

NOVEMBER 19, 2024

Implants

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AT A GLANCE

This page includes recommendations for health care providers that address provision and use of implants. This information comes from the 2024 U.S. Selected Practice Recommendations for Contraceptive Use (U.S. SPR).

Overview

The ENG implant, a single rod with 68 mg of ENG, is available in the United States. Fewer than one implant user out of 100 become pregnant in the first year with typical use.^[28] The implant is long acting, is reversible, and can be used by patients of all ages, including adolescents. The implant does not protect against STIs, including HIV infection, and patients using the implant should be counseled that consistent and correct use of external (male) latex condoms reduces the risk for STIs, including HIV infection.^[31] Use of internal (female) condoms can provide protection from STIs, including HIV infection, although data are limited.^[31] Patients also should be counseled that PrEP, when taken as prescribed, is highly effective for preventing HIV infection.^[32]

Initiation of implants

Timing

The implant may be placed at any time if it is reasonably certain that the patient is not pregnant (Box 3).

Need for Back-Up Contraception

- If the implant is placed within the first 5 days since menstrual bleeding started, no additional contraceptive protection is needed.
- If the implant is placed >5 days since menstrual bleeding started, the patient needs to abstain from sexual intercourse or use barrier methods (e.g., condoms) for the next 7 days.

Special Considerations

Amenorrhea (Not Postpartum)

- Timing: The implant may be placed at any time if it is reasonably certain that the patient is not pregnant (Box 3).
- Need for back-up contraception: The patient needs to abstain from sexual intercourse or use barrier methods (e.g., condoms) for the next 7 days.



Postpartum (Breastfeeding)

- Timing: The implant may be placed at any time (U.S. MEC 2 if <30 days postpartum and U.S. MEC 1 if ≥30 days postpartum), if it is reasonably certain that the patient is not pregnant (Box 3).^[1]
- Need for back-up contraception: If the patient is <6 months postpartum, amenorrheic, and fully or nearly fully breastfeeding (exclusively breastfeeding or the vast majority [≥85%] of feeds are breastfeeds), no additional contraceptive protection is needed.^[44] Otherwise, a patient who is ≥21 days postpartum and whose menstrual cycle has not returned needs to abstain from sexual intercourse or use barrier methods (e.g., condoms) for the next 7 days. If the patient's menstrual cycle has returned and it has been >5 days since menstrual bleeding started, the patient needs to abstain from sexual intercourse or use barrier methods (e.g., condoms) for the next 7 days.

Postpartum (Nonbreastfeeding)

• Timing: The implant may be placed at any time, including immediately postpartum (U.S. MEC 1), if it is reasonably certain that the patient is not pregnant (Box 3).^[1]

Need for back-up contraception: If the patient is <21 days postpartum, no additional contraceptive protection is needed. A patient who is ≥21 days postpartum and whose menstrual cycle has not returned needs to abstain from sexual intercourse or use barrier methods (e.g., condoms) for the next 7 days. If the patient's menstrual cycle has returned and it has been >5 days since menstrual bleeding started, the patient needs to abstain from sexual intercourse or use barrier methods (e.g., condoms) for the next 7 days.

Postabortion (Spontaneous or Induced)

- **Timing:** The implant may be placed at any time postabortion, including immediately after abortion completion, if it is reasonably certain that the patient is not pregnant (<u>Box 3</u>), or at time of medication abortion initiation (U.S. MEC 1).^[1]
- Need for back-up contraception: The patient needs to abstain from sexual intercourse or use barrier methods (e.g., condoms) for the next 7 days unless the implant is placed at the time of an abortion.

Switching From Another Contraceptive Method

- **Timing:** The implant may be placed immediately if it is reasonably certain that the patient is not pregnant (<u>Box 3</u>). Waiting for the patient's next menstrual cycle is unnecessary.
- Need for back-up contraception: If it has been >5 days since menstrual bleeding started, the patient needs to abstain from sexual intercourse or use barrier methods (e.g., condoms) for the next 7 days.
- Switching from an IUD: In addition to the need for back-up contraception when starting the implant, there might be additional concerns when switching from an IUD. If the patient has had sexual intercourse since the start of their current menstrual cycle and it has been >5 days since menstrual bleeding started, theoretically, residual sperm might be in the genital tract, which could lead to fertilization if ovulation occurs. A health care provider may consider any of the following options to address the potential for residual sperm:
 - Advise the patient to retain the IUD for at least 7 days after the implant is placed and return for IUD removal.
 - Advise the patient to abstain from sexual intercourse or use barrier methods (e.g., condoms) for 7 days before removing the IUD and switching to the new method. If it has been >5 days since menstrual bleeding started, the patient needs to abstain from sexual intercourse or use barrier methods (e.g., condoms) for the next 7 days.
 - If the patient cannot return for IUD removal and has not abstained from sexual intercourse or used barrier methods (e.g., condoms) for 7 days, advise the patient to use ECPs (with the exception of UPA) at the time of IUD removal. If it has been >5 days since menstrual bleeding started, the patient needs to abstain from sexual intercourse or use barrier methods (e.g., condoms) for the next 7 days.

Comments and Evidence Summary

In situations in which the health care provider is uncertain whether the patient might be pregnant, the benefits of starting the implant likely exceed any risk. Therefore, starting the implant should be considered at any time, with a follow-up pregnancy test in 2–4 weeks. If a patient needs to use additional contraceptive protection when switching to an implant from another contraceptive method, consider continuing their previous method for 7 days after implant placement. (As appropriate, see recommendations for <u>Emergency Contraception</u>.)

No direct evidence was found regarding the effects of starting the ENG implant at different times of the cycle.

Examinations and tests needed before implant initiation

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Among healthy patients, no examinations or tests are needed before initiation of an implant, although a baseline weight and BMI measurement might be useful for addressing any concerns about changes in weight over time (<u>Table 2</u>). Patients with known medical problems or other special conditions might need additional examinations or tests before being determined to be appropriate candidates for a particular method of contraception. U.S. MEC might be useful in such circumstances.^[1]

Table 2. Classification of examinations and tests needed before implant initiation	+
Examination or test	Class*
Examination	
Blood pressure	С
Weight (BMI) (weight [kg]/height [m] ²)	t
Clinical breast examination	С
Bimanual examination and cervical inspection	С
Laboratory test	

Examination or test	Class*
Glucose	С
Lipids	С
Liver enzymes	С
Hemoglobin	С
Thrombophilia	С
Cervical cytology (Papanicolaou smear)	С
STI screening with laboratory tests	С
HIV screening with laboratory tests	С

Abbreviations: BMI = body mass index; STI = sexually transmitted infection; U.S. MEC = *U.S. Medical Eligibility Criteria for Contraceptive Use.*

* Class A: Essential and mandatory in all circumstances for safe and effective use of the contraceptive method.

Class B: Contributes substantially to safe and effective use, but implementation may be considered within the public health context, service context, or both; the risk of not performing an examination or test should be balanced against the benefits of making the contraceptive method available.

Class C: Does not contribute substantially to safe and effective use of the contraceptive method. (Source: World Health Organization. Selected practice recommendations for contraceptive use, 2nd ed. Geneva, Switzerland: WHO Press; 2004.)

[†] Weight (BMI) measurement is not needed to determine medical eligibility for any methods of contraception because all methods can be used (U.S. MEC 1) or generally can be used (U.S. MEC 2) among patients with obesity (BMI \geq 30 kg/m²). However, measuring weight and calculating BMI at baseline might be helpful for discussing concerns about any changes in weight and whether changes might be related to use of the contraceptive method.

Comments and Evidence Summary

Weight (BMI): Patients with obesity (BMI \geq 30 kg/m²) can use implants (U.S. MEC 1); therefore,^[1] screening for obesity is not necessary for the safe initiation of implants. However, measuring weight and calculating BMI at baseline might be helpful for discussing concerns about any changes in weight and whether changes might be related to use of the contraceptive method.

Bimanual examination and cervical inspection: A pelvic examination is not necessary before initiation of implants because it would not facilitate detection of conditions for which implant use would be unsafe. Although patients with certain conditions or characteristics should not use (U.S. MEC 4) or generally should not use (U.S. MEC 3) implants, none of these conditions are likely to be detected by pelvic examination.^{[1], [172]} A systematic review identified two case-control studies that compared delayed and immediate pelvic examination before initiation of hormonal contraceptives, specifically oral contraceptives or DMPA.^[23] No differences in risk factors for cervical neoplasia, incidence of STIs, incidence of abnormal Papanicolaou smears, or incidence of abnormal wet mounts were observed. No evidence was found regarding implants (Level of evidence: II-2 fair, direct).

Lipids: Screening for dyslipidemias is not necessary for the safe initiation of implants because of the low likelihood of clinically significant changes with use of hormonal contraceptives. A systematic review did not identify any evidence regarding outcomes among women who were screened versus not screened with lipid measurement before initiation of hormonal contraceptives.^[24] During 2015–2016, among women aged 20–39 years in the United States, 6.7% had high cholesterol, defined as total serum cholesterol >240 mg/dL.^[111] Studies have reported mixed results regarding the effects of hormonal methods on lipid levels among both healthy women and women with baseline lipid abnormalities, and the clinical significance of these changes is unclear.^[112-115]

Liver enzymes: Although patients with hepatocellular carcinoma generally should not use implants (U.S. MEC 3), patients with benign liver

tumors, viral hepatitis, or cirrhosis can use (U.S. MEC 1) or generally can use (U.S. MEC 2) implants; screening for liver disease before initiation of implants is not necessary because of the low prevalence of these conditions and the high likelihood that patients with liver disease already would have had the condition diagnosed.^[1] A systematic review did not identify any evidence regarding outcomes among women who were screened versus not screened with liver enzyme tests before initiation of hormonal contraceptives.^[24] During 2012, the percentage of U.S. women with liver disease (not further specified) was 1.3%.^[116] During 2013, the incidence of acute hepatitis A, B, or C was ≤ 1 per 100,000 U.S. population.^[117] During 2002–2011, the incidence of liver cancer among U.S. women was approximately 3.7 per 100,000 population.^[118]

Clinical breast examination: Although patients with current breast cancer should not use implants (U.S. MEC 4), screening asymptomatic patients with a clinical breast examination before initiation of implants is not necessary because of the low prevalence of breast cancer among women of reproductive age (15–49 years).^[1] A systematic review did not identify any evidence regarding outcomes among women who were screened versus not screened with a breast examination before initiation of hormonal contraceptives.^[23] The incidence of breast cancer among women of reproductive age in the United States is low. During 2020, the incidence of breast cancer among women aged <50 years was approximately 45.9 per 100,000 women.^[119]

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Other screening: Patients with hypertension, diabetes, iron-deficiency anemia, thrombophilia, cervical intraepithelial neoplasia, cervical cancer, STIs, or HIV infection can use (U.S. MEC 1) or generally can use (U.S. MEC 2) implants.^[1] Therefore, screening for these conditions is not necessary for the safe initiation of implants.

Routine follow-up after implant placement

These recommendations address when routine follow-up is needed for safe and effective continued use of contraception for healthy patients. The recommendations refer to general situations and might vary for different users and different situations. Specific populations who might benefit from more frequent follow-up visits include adolescents, those with certain medical conditions or characteristics, and those with multiple medical conditions.

- Advise the patient that they may contact their provider at any time to discuss side effects or other problems, if they want to change the method being used, and when it is time to remove or replace the contraceptive method. No routine follow-up visit is required.
- At other routine visits, health care providers seeing implant users should do the following:
 - Assess the patient's satisfaction with their contraceptive method and whether they have any concerns about method use.
 - Assess any changes in health status, including medications, that would change the appropriateness of the implant for safe and effective continued use on the basis of U.S. MEC (e.g., category 3 and 4 conditions and characteristics).^[1]
 - Consider assessing weight changes and discussing concerns about any changes in weight and whether changes might be related to use of the contraceptive method.

Comments and Evidence Summary

A systematic review did not identify any evidence regarding whether a routine follow-up visit after initiating an implant improves correct or continued use.^[22]

Bleeding irregularities (including amenorrhea) during implant use

Before implant placement, provide counseling about potential changes in bleeding patterns during implant use. Spotting or light bleeding is
common with implant use, and certain implant users experience amenorrhea. These bleeding changes are generally not harmful but might be
bothersome to the patient. Bleeding changes might or might not decrease with continued implant use. Heavy bleeding is uncommon during
implant use.

Bleeding Irregularities (Spotting, Light Bleeding, or Heavy or Prolonged Bleeding)

- If clinically indicated, consider an underlying health condition, such as interactions with other medications, STIs, pregnancy, thyroid disorders, or new pathologic uterine conditions (e.g., polyps or fibroids). If an underlying health condition is found, treat the condition or refer for care.
- Explore patient goals, including continued implant use (with or without treatment for bleeding irregularities) or implant removal. If the patient wants to continue implant use, provide reassurance, discuss options for management of bleeding irregularities if it is desired, and advise the patient that they may contact their provider at any time to discuss bleeding irregularities or other side effects.
- If the patient desires implant removal at any time, remove the implant, offer counseling on alternative contraceptive methods, and initiate another method if it is desired.
- If the patient wants treatment, the following treatment options may be considered, depending on the patient's preferences, treatment goals, and medical history:
 - Treatments that might improve bleeding irregularities during treatment use; bleeding is likely to recur after treatment cessation. Treatment may be repeated as needed.
 - Hormonal treatment (e.g., $20-30 \ \mu g \ EE \ COCs$ or estrogen).
 - Antifibrinolytic agents (e.g., tranexamic acid), 5 days.
 - Treatments that might improve bleeding irregularities during treatment use and whose effects might persist for some time after treatment cessation. Treatment may be repeated as needed.

- NSAIDs (e.g., celecoxib, ibuprofen, or mefenamic acid), 5-7 days.

- SERMs (e.g., tamoxifen), 7-10 days.

Amenorrhea

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- Amenorrhea does not require any medical treatment. Provide reassurance.
 - If a patient's regular bleeding pattern changes abruptly to amenorrhea, consider ruling out pregnancy if clinically indicated.
- If the patient desires implant removal, remove the implant, offer counseling on alternative contraceptive methods, and initiate another method if it is desired.

Comments and Evidence Summary

During contraceptive counseling and before placement of the implant, information about common side effects, such as spotting or light bleeding and amenorrhea, especially during the first year of use, should be discussed. A pooled analysis of data from 11 clinical trials indicates that a significant proportion of ENG implant users had relatively little bleeding: 22% of women experienced amenorrhea and 34% experienced infrequent spotting, although 7% reported frequent bleeding and 18% reported prolonged bleeding.^[173] Bleeding or amenorrhea is generally not harmful but might be bothersome to the patient. Enhanced counseling about expected bleeding patterns and reassurance that bleeding irregularities are generally not harmful has been demonstrated to reduce method discontinuation in clinical trials with other hormonal contraceptives (i.e., DMPA).^{[147],[148]}

For patients seeking care for bleeding irregularities while using an implant, it is important to explore patient goals, including removal of the implant, treatment for bleeding irregularities, or continued use of the implant without treatment. Irregular bleeding during contraceptive implant use might be caused by several mechanisms, including an atrophic endometrium, dysregulated angiogenesis, increased matrix metalloproteinase activity, or increased expression of prostaglandin metabolites.^[174-178] Multiple treatments have been evaluated to manage irregular bleeding with implant use, which have different proposed mechanisms of action and likely different effects.

- NSAIDs decrease prostaglandin levels and might reduce menstrual blood loss. [179]
- Estrogen alone or estrogen-containing contraception has been used to help stabilize the endometrium and was initially proposed as bleeding episodes in LNG implant users were associated with low serum estradiol levels.^{[180],[181]}
- SERMs and selective progesterone receptor modulators (SPRMs) (e.g., tamoxifen, mifepristone, and UPA) might modulate endometrial angiogenesis and endometrial proliferation. [175], [182-186]
- Tranexamic acid is an antifibrinolytic agent.^[187]
- Doxycycline has been investigated because of its ability to inhibit matrix metalloproteinases. [188], [189]
- Certain treatments, such as estrogen alone or estrogen-containing contraception, likely work to decrease bleeding primarily during treatment use, whereas other drugs, such as NSAIDs, SERMs, and SPRMs, might have effects that continue after treatment is completed.
- Evidence is limited on specific drugs, doses, and durations of use for effective treatments for bleeding irregularities with ENG implant use. Therefore, this report includes general recommendations for treatments to consider rather than specific regimens.

Although the ENG implant is the only implant available in the United States, evidence from studies of both ENG and LNG implants was considered for this recommendation because the mechanisms for bleeding irregularities with both implants are similar.^[190] Evidence includes nine RCTs that examined treatments for bleeding irregularities with ENG implants and 11 RCTs that investigated treatments for bleeding irregularities with LNG implants; in addition, one placebo-controlled trial with a nonrandom method of allocation (i.e., assigned systematically, in sequence of enrollment) is described because of its historical inclusion in the evidence for this recommendation (Supplementary Appendix, https://stacks.cdc.gov/view/cdc/156517). Trials primarily reported on outcomes related to improvements in bleeding irregularities; few trials reported any side effects or adverse events. Few trials reported on patient satisfaction or implant discontinuation.

NSAIDs. *Celecoxib:* One small study among LNG implant users found higher proportions of participants experienced cessation of bleeding within 7 days of start of treatment as well as fewer bleeding and spotting days after treatment cessation and a longer bleed-free interval in 28 days of follow-up with oral celecoxib (200 mg) daily for 5 days compared with placebo.^[191] No trials investigated celecoxib use among ENG implant users (Certainty of evidence: high).

Mefenamic acid: Two trials examined mefenamic acid; one was conducted among LNG implant users who took oral mefenamic acid (500 mg) two times daily and one among ENG implant users who took mefenamic acid (500 mg) three times daily.^{[192],[193]} Both trials found higher proportions of participants experienced cessation of bleeding within 7 days of start of treatment and improved bleeding patterns after treatment cessation in 28 days of follow-up among implant users taking mefenamic acid for 5 days compared with placebo.^{[192],[193]} However, a head-to-head trial demonstrated greater cessation of bleeding within 7 days of start of treatment for daily use of a 20 µg EE/150 µg desogestrel COC compared with a course of mefenamic acid (500 mg) 3 times daily for 5 days among ENG implant users ^[194] (Certainty of evidence for mefenamic acid: high; certainty of evidence for mefenamic acid versus COC: very low).

Ibuprofen: Ibuprofen use among LNG implant users demonstrated inconsistent effects. One trial did not demonstrate any significant differences in the number of bleeding and spotting days after a course of ibuprofen (800 mg) twice daily for 5 days compared with placebo. ^[195] Another trial with a nonrandom method of allocation (i.e., assigned systematically, in sequence of enrollment) reported a reduction in number of bleeding and spotting days after initiating ibuprofen (800 mg) 3 times daily for 5 days compared with placebo. ^[196] No trials investigated ibuprofen use among ENG implant users (Certainty of evidence: very low to low).

Antifibrinolytic agents. *Tranexamic acid:* Tranexamic acid (500 mg) twice daily for 5 days among LNG implant users increased the percentage of those who stopped bleeding within 7 days of treatment initiation compared with placebo. However, there was no difference in bleeding and spotting days after treatment cessation in the 28-day follow-up period between those using tranexamic acid and those using placebo.^[197] No trials investigated tranexamic acid among ENG implant users (Certainty of evidence: high).

Hormonal treatment. *COCs:* COC courses ranging from 14 to 42 days decreased bleeding on treatment compared with placebo in both LNG and ENG implant users but did not improve bleeding after treatment cessation.^[198-201] Three trials compared a 30 µg EE/150 µg LNG pill with placebo [two among ENG implant users and one among LNG implant users], whereas a study among LNG users compared a 50 µg EE/250 µg LNG pill with placebo.^{[199],[200],[201]} In addition, a 20 µg EE/150 µg desogestrel COC improved time to bleeding episode cessation compared with mefenamic acid among ENG implant users ^[194] (Certainty of evidence for COCs: very low to high; certainty of evidence for COC versus mefenamic acid: low).

Estrogen: EE use among LNG implant users decreased bleeding on treatment compared with placebo but had inconsistent effects on bleeding patterns after treatment completion. In two RCTs and one trial with a nonrandom method of allocation (i.e., assigned systematically, in sequence of enrollment), EE (50 μg) daily for approximately 3 weeks decreased bleeding and spotting while on treatment, but off-treatment effects were inconsistent;^{[198],[201]} only the nonrandomized trial reported decreased bleeding and spotting days after treatment cessation for EE (50 μg) users compared with placebo.^[196] EE (20 μg) for 10 days^[195] and use of an estradiol patch (100 μg/day releasing) for 6 weeks did not improve bleeding irregularities compared with placebo.^[202] No trials investigated use of EE among ENG implant users (Certainty of evidence for oral EE [50 μg]: very low to moderate; certainty of evidence for oral EE [20 μg] and estradiol patch: very low).

SERMs. *Tamoxifen:* One trial of tamoxifen (10 mg) twice daily for 10 days observed decreased bleeding during and after treatment compared with placebo for LNG implant users.^[203] Two trials using tamoxifen (10 mg) twice daily for 7 days among ENG implant users observed decreased bleeding and spotting days and increased bleed-free interval after treatment cessation compared with placebo^{[204],} [205] (Certainty of evidence: high).

Additional interventions for which evidence suggested no positive effect or evidence was too limited to make a recommendation: Evidence on multiple other interventions was identified, including aspirin (one trial),^[206] LNG pills (one trial),^[196] mifepristone (three trials), ^[207–209] UPA (one trial),^[210] doxycycline alone (two trials),^{[208],[209]} doxycycline combined with EE (one trial),^[209] doxycycline combined with mifepristone (one trial),^[209] and vitamin E (two trials).^{[206],[211]} For these interventions, the evidence either suggested no positive effect on the outcomes assessed or the evidence was too limited to make a recommendation. A detailed summary of the evidence is provided (Supplementary Appendix, <u>https://stacks.cdc.gov/view/cdc/156517</u>).

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