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Tips for Clinicians

Implanon: The Subdermal Contraceptive Implant

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Introduction

Subdermal progestin implants provide highly effective contraception with minimal doses of hormone and require little effort for compliance. Implants may be a good first-line birth control choice for adolescents, in whom discreet, effective protection is desired and compliance with other contraceptive methods is suboptimal. Progestin implants may also be a contraceptive option for young women who cannot use other methods, including women with comorbid medical conditions who may have contraindications to estrogen. Finally, subdermal implants are a good choice for any woman who desires long- term, effective protection from pregnancy without needing to adhere to a schedule or to initiate the method at the time of intercourse.

What is Implanon?

Implanon (Merck & Co, Inc) is a single rod subdermal implant containing 68 mg of the progestin etonogestrel, the active metabolite of desogestrel.[1] The product has been available worldwide since 1999 and in Australia since 2001. It was approved for use in the United States in 2006. The contraceptive rod is 4 cm in length and 2 mm in diameter, with a release rate-controlling membrane of ethylene vinyl acetate.[2] Implanon provides contraception for up to three years.[1,3] Preloaded, disposable, sterile applicators are provided for easy, subdermal insertion. The Implanon is placed subdermally, in the medial aspect of the non-dominant arm, 6 to 8 cm above the elbow.[2] The rod should be easily palpable under the skin. Training is required for insertion and removal. Implanon is removed by making a 2-mm incision near the tip of the rod and removing the rod with forceps. Implanon rods that cannot be palpated can be imaged using ultrasound (at least 10 MHz, using a linear array transducer and a transverse scan technique) or MRI. The device is not radio-opaque.[2,4] The average insertion time is 0.5 minutes (range, 0.05 to 15 minutes) and average removal time is 3.5 minutes (range, 0.2 to 60 minutes); insertion and removal times improve with experience.[2]

How does Implanon Work?

Implanon prevents pregnancy primarily by suppressing ovulation.[3] A release rate of 25-30 μg/day of etonogestrel is required to suppress ovulation.[5] The etonogestrel in Implanon is released at an initial rate of approximately 60–70 μg/day, which slowly decreases to about 30 μg/day by years 2 and 3.[6] Implanon also causes thickening of the cervical mucous so that it becomes impenetrable to sperm, and causes the endometrial lining to become thin and atrophic.[7]

Implanon has a Pearl Index of 0.00–0.07.[8] In clinical trials, there was one pregnancy in over 70,000 cycles.[9] A post marketing surveillance study in Australia done three years after Implanon had been in use estimated a failure rate of 1 out of 1000 (0.1%).[10] This study included over 200,000 insertions and demonstrated only 13 product or method failures. Of the 218 confirmed unintended pregnancies associated with Implanon, 21% of cases had insufficient data to determine the reason for the unintended pregnancy. In another 21% of the 218 cases the woman was already pregnant before Implanon was inserted. In these cases, either a pregnancy test was not performed, or the pregnancy test was still negative, due to the woman being in the very early stages of pregnancy. ''Non-insertion'' of the Implanon rod was documented in 39% of the cases. For example, the rod was found left in the applicator, or a placebo Implanon from a training pack was inserted by mistake. Interaction between Implanon and other medications was thought to be the cause of failure in 4% of cases. All drug interactions identified involved antiepileptic drugs; seven of the eight patients with unintended pregnancy due to drug interaction were taking carbamazepine.

Timing of Insertion

Insertion of Implanon should be scheduled at a time when one can be as certain as possible that the

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BOX 1. Appropriate Insertion Times for Implanon[11]

- No use of hormones: cycle day 1−5
- Changing from combination oral contraceptives: after last active pill, before completion of placebos
- Changing from progestin-only pill/injectable/implant: immediately
- Post- partum: day 21−28 after delivery

with later insertion, exclude pregnancy and use additional contraceptive method for seven days.

woman is not pregnant. A pregnancy test should always be performed. Insertion can occur at any time in the cycle, but when administered at certain times, Implanon will be immediately effective and the patient is not required to use an additional form of contraception. If a patient is currently not using birth control and is cycling regularly, Implanon may be inserted on cycle day one through cycle day five, with cycle day one being the first day of bleeding. If a patient is currently on combination oral contraceptives, Implanon should be inserted after the last active hormone pill, and before the last placebo pill is taken. If the patient is switching to Implanon from a different progestin-only contraceptive, such as Depo Provera, another implant, progestin IUD, or progestin-only contraceptive pills, Implanon can be inserted at any time. In the postpartum patient, Implanon should be inserted on day 21 through day 28 after delivery.[11] These recommendations are summarized in Box 1.

In women who are not using any hormonal contraception and insertion has not occurred in the first five days of the menstrual cycle, or in women with irregular cycles, pregnancy must be excluded with a urine pregnancy test. If a woman reports unprotected intercourse within the prior two weeks, two pregnancy tests should be performed: the first at the initial visit, and if negative, the second two weeks later. She needs to abstain from intercourse during these two weeks, or use a barrier form of contraception properly. In two weeks, if a second pregnancy test is negative, Implanon can be inserted. She should use another form of contraception for the next seven days, in case ovulation occurred just prior to insertion.[11] Within hours of insertion serum progestin levels rise and cervical mucous changes are detectable.[7]

Side Effects and Acceptability

The most common side effect reported is abnormal bleeding.[12] Overall, bleeding is decreased, but the pattern is variable, and unfortunately, it is not possible to predict the bleeding pattern for any individual. A wide range of bleeding patterns is experienced in adult users of Implanon. Women can be counseled that overall, in the 90-day reference periods of clinical trial experience, 33.3% had infrequent bleeding, 21.4% had amenorrhea, 6.1% had frequent bleeding, and 16.9% had prolonged bleeding.[13]

Other reported side effects of Implanon include acne, weight gain, mood changes, and headache. Because etonogestrel has a lower androgenic effect, the side effects of acne and weight gain are reported less frequently than with other progestins. In a large multicenter study of Implanon in Europe and South America, 12.8% of women reported improvement in acne with Implanon, while 12.6% reported new or worsened acne. In the same trial, the mean body mass index (BMI) increased greater than 10% above baseline in 20.2% of women. The mean percent increase in BMI was 3.5% .[1] A clinical review identified a clinically significant weight gain in 21% of Implanon users.[14] An integrated analysis of data from 13 studies demonstrated an average increase of 2.6% in body weight over a two-year period among Implanon users. This average weight increase was not significantly different from controls who were using non-hormonal methods.[15] Local skin irritation is the most common insertion site problem and occurs in about 5% of women.[7] Implanon users report a significant improvement in dysmenorrhea during Implanon use.[12]

No studies directly evaluate teen acceptance of Implanon. Information from a U.S. study of 56 adolescents choosing Norplant compared to 56 choosing the oral contraceptive pill showed that despite 73% of adolescents using Norplant reporting menstrual irregularities, 1-year continuation rates for Norplant were 91/100, compared to 34% for the pill.[16]

Discontinuation of Implanon

Rates of discontinuation have varied geographically, with the highest discontinuation rates of 30.2% by three years in Europe and Canada, and lower rates of discontinuation in South East Asia of 0.9%.[12] The rate of discontinuation tended to be highest in the first year of use, with an average expected rate of discontinuation of about 20% the first year.[1,17] Cultural variations probably explain the differences in acceptability of the method. In some cultures, irregular bleeding is more acceptable, and some women are willing to tolerate more side effects in order to avoid pregnancy. Additionally, many other practical reasons affect acceptability and continuation of a method, including how badly contraception is desired, access to