Implanon NXT™
68 mg etonogestrel

GLOBAL TRAINING

IMPLANON NXT™: Reference Guide

IMPLANON NXT™ (etonogestrel implant): Clinical Information

A double-blind, parallel-group, randomized trial in 108 women has conclusively shown that IMPLANON and IMPLANON NXT are bioequivalent. Therefore, the trial data for IMPLANON NXT used to support the statements made throughout this document are accurate and relevant for both products.

- IMPLANON NXT is a subdermal, long-acting, progestagen-only contraceptive effective for up to 3 years.
- IMPLANON NXT is radiopaque and comparable to IMPLANON™ (etonogestrel implant).[1]
- The mechanisms of action of IMPLANON NXT consist of inhibition of ovulation and increases in the viscosity of cervical mucus.
- Efficacy does not depend on daily, weekly, or monthly self-administration.
  - IMPLANON NXT is effective from day one, when inserted according to instructions in the label.
- No method of contraception is 100% effective – IMPLANON and IMPLANON NXT have been shown to be over 99% effective when inserted correctly. [2]
  - Studies show a continuation rate of 82% after 1 year of use. [3]
  - 11% of women studied discontinued IMPLANON due to bleeding irregularities.
  - Bleeding irregularities may include amenorrhea or infrequent, frequent, and/or prolonged bleeding. Information, counseling, and the use of a bleeding diary can improve the woman's acceptance of a bleeding pattern.
- Following removal of IMPLANON NXT, the hormone is below detectable levels within 7 days.[4]

Bone Mineral Density

- A comparative study of IMPLANON and a non-hormonal IUD showed that bone mineral density remained unaltered over 2 years, with no detectable difference between users of each contraceptive method.

Breast Milk

- In clinical studies, indicate that IMPLANON NXT does not influence the quantity or quality (protein, lactose, or fat concentrations) of breast milk in nursing mothers. However, small amounts of etonogestrel are excreted in breast milk.
- Evaluation of growth and physical and psychomotor development of 38 children breast-fed for an average of 14 months did not indicate any differences in comparison to nursing infants whose mothers used an IUD (n=33); each group was followed-up to 36 months of age. Based on the available data, IMPLANON NXT may be used during lactation and should be inserted after the 4th postpartum week.

Adverse Events

- Headache
- Weight increase
- Acne
- Breast pain
- Irregular menstruation
- Vaginal infections

Please refer to the regulatory-approved full Prescribing Information for complete list of adverse events.

Contraindications

- Use of IMPLANON NXT is contraindicated in patients with:
  - Known or suspected pregnancy
  - Active venous thromboembolic disorder
  - Known or suspected sex steroid-sensitive malignancies
  - Presence of history of liver tumors (benign or malignant)
  - Presence or history of severe hepatic disease as long as liver function values have not returned to normal
  - Undiagnosed vaginal bleeding
  - Hypersensitivity to the active substance or to any of the excipients of IMPLANON NXT

Interactions

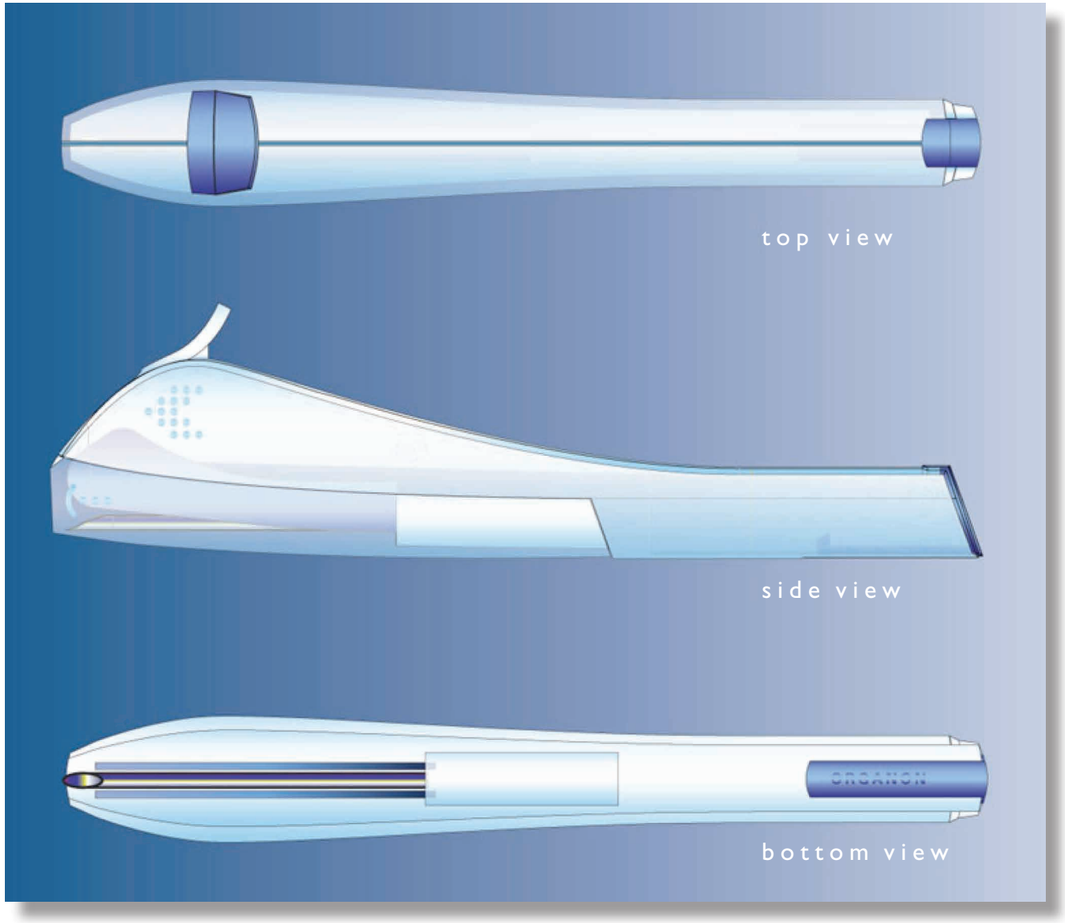
- The Prescribing Information of concomitant medications used by the patient should be consulted to identify potential interactions.
- Interactions can occur with medicinal products that induce hepatic enzymes, specifically cytochrome P450 enzymes, which can result in increased clearance of sex hormones (eg, phenytoin, phenobarbital, primidone, bosentan, carbamazapine, rifampicin, and HIV medication [eg, ritonavir, nelfinavir, nevirapine], and possibly also oxcarbazepine, topiramate, felbamate, griseofulvin, and the herbal remedy St. John's wort). Also, HIV protease (eg, ritonavir, nelfinavir), non-nucleoside reverse transcriptase inhibitors (eg, nevirapine, efavirenz), and combinations of them have been reported to potentially affect hepatic metabolism.
  - Women on treatment with any of the above mentioned drugs should use a non-hormonal contraceptive method in addition to IMPLANON NXT.

Please refer to the regulatory-approved full Prescribing Information for additional interactions.

Pregnancy

- IMPLANON NXT is not indicated during pregnancy. If pregnancy occurs during use of IMPLANON NXT, the implant should be removed.
- Animal studies have shown that very high doses of progestagenic substances may cause masculinization of female fetuses. Extensive epidemiological studies have revealed neither an increased risk of birth defects in children born to women who used oral contraceptives (OCs) prior to pregnancy, nor a teratogenic effect when OCs were inadvertently used during pregnancy. Although this probably applies to all OCs, it is not clear whether this is also the case for IMPLANON NXT.

Applicator for IMPLANON NXT™



Key Points for Patient Counseling

- Women are likely to have changes in their menstrual bleeding pattern with IMPLANON NXT. These may include changes in bleeding frequency, intensity, or duration; however, the bleeding pattern experienced during the first 3 months is broadly predictive of future bleeding patterns for many women.
- Amenorrhea was reported in about 1 of 5 women, while another 1 of 5 women reported frequent and/or prolonged bleeding.
- Dysmenorrhea tended to improve while using IMPLANON NXT.
- Appropriate counseling may make bleeding changes more acceptable for women.
- Key counseling points include:
  - Discussion of the likelihood of alterations in bleeding patterns
  - Discussion of the risks, benefits, and possible side effects
- Explain the insertion and removal procedures; emphasizing that the implant should be palpable and that scars or complications may occur.
- If possible, provide patient education materials.
- Allow sufficient time for the patient to review the regulatory-approved Patient Information and Prescribing Information, consider options, and ask questions.

References: 1 – Schnabel 2012, 2 – Graesslin 2008, 3 – Blumenthal 2008, 4 – Davies 1993

How to Insert IMPLANON NXT™

Figure 1

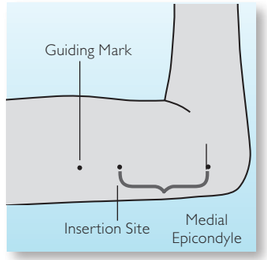


Figure 2

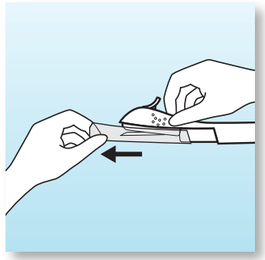


Figure 3

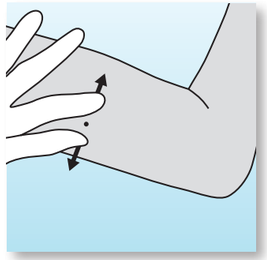


Figure 4

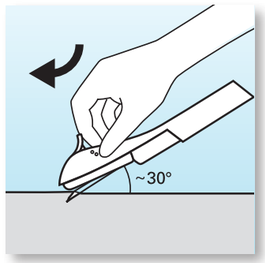


Figure 5

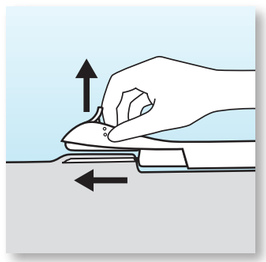


Figure 6

Figure 7

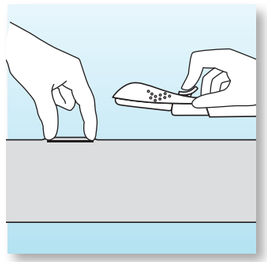


Figure 8

- Insertion of IMPLANON NXT should be performed under aseptic conditions and only by a qualified health care provider who is familiar with the procedure. Insertion of the implant should only be performed with the preloaded applicator strictly in accordance with the insertion instructions outlined in the regulatory-approved Prescribing Information.
- It is recommended that the health care provider is in a seated position during the entire insertion procedure so that the insertion site and the movement of the needle can be clearly seen.
- Have the woman lie on her back on the examination table with her non-dominant arm flexed at the elbow and externally rotated so that her wrist is parallel to her ear or her hand is positioned next to her head (Figure 1).
- Identify the insertion site, which is at the inner side of the non-dominant upper arm about 8 to 10 cm (3 to 4 inches) above the medial epicondyle of the humerus.

The implant should be inserted subdermally just under the skin to avoid the large blood vessels and nerves that lie deeper in the subcutaneous tissue in the sulcus between the triceps and biceps muscles.

- Make 2 marks with a sterile marker; first, mark the spot where the implant will be inserted, and second, mark a spot a few centimeters proximal to the first mark (Figure 2). This second mark will later serve as a direction guide during insertion.
- Clean the insertion site with an antiseptic solution.
- Anesthetize the insertion area (for example with anesthetic spray or by injecting 2 mL of 1% lidocaine just under the skin along the planned insertion tunnel).
- Remove the sterile preloaded disposable applicator for IMPLANON NXT carrying the implant from its blister.
- Hold the applicator just above the needle at the textured surface area and remove the transparent protection cap from the needle which contains the implant (Figure 3).
- If the cap does not come off easily, the applicator should not be used. You may see the white-colored implant by looking into the tip of the needle.

Do not touch the purple slider until you have fully inserted the needle subdermally, as it will retract the needle and release the implant from the applicator.

- With your free hand, stretch the skin around the insertion site with thumb and index finger (Figure 4).
- Puncture the kin with the tip of the needle angled about 30° (Figure 5).
- Lower the applicator to a horizontal position. While lifting the skin with the tip of the needle, slide the needle to its full length. You may feel slight resistance but do not exert excessive force (Figure 6).

If the needle is not inserted to its full length, the implant will not be inserted properly.

- While keeping the applicator in the same position and the needle inserted to its full length, unlock the purple slider by pushing it slightly down. Move the slider fully back until it stops, leaving the implant now in its final subdermal position and locking the needle inside the body of the applicator (Figure 7).

If the applicator is not kept in the same position during this procedure or if the purple slider is not completely moved to the back, the implant will not be inserted properly.

- **Always verify the presence of the implant in the woman's arm immediately after insertion by palpation.** By palpating both ends of the implant, you should be able to confirm the presence of the 4 cm rod (Figure 8).

If you cannot feel the implant or doubt its presence:

- Check the applicator. The needle should be fully retracted and only the purple tip of the obturator should be visible.
- Use other methods to confirm its presence. Suitable methods are: 2-dimensional X-ray, X-ray computerized tomography (CT scan), ultrasound scanning (USS) with a high-frequency linear array transducer (10 MHz or greater), or magnetic resonance imaging (MRI).

Prior to the application of X-ray CT, USS, or MRI for the localization of the implant, it is recommended to consult the local supplier of IMPLANON NXT for instructions.

In case these imaging methods fail, it is advised to verify the presence of the implant by measuring the etonogestrel level in a blood sample of the subject. In this case, the local supplier will provide the appropriate procedure. **Until you have verified the presence of the implant, a non-hormonal contraceptive method must be used.**

- Apply a small adhesive bandage over the insertion site. Request that the woman palpate the implant.
- Apply sterile gauze with a pressure bandage to minimize bruising. The woman may remove the pressure bandage in 24 hours and the small bandage over the insertion site after 3 to 5 days.
- Complete the User Card and give it to the woman to keep. Complete the adhesive labels and affix to the woman's medical record.
- The applicator is for single use only and must be adequately disposed of, in accordance with local regulations for the handling of biohazardous waste.

Localizing IMPLANON NXT™

- Localization is an essential component of the insertion and removal process. Palpation is the first step in the localization process.

  Always localize by palpation:
  - Immediately after insertion
  - Immediately prior to removal
- If the patient has retained and can provide a completed User Card, review it to determine:
  - Whether the implant is radiopaque (IMPLANON NXT) or not radiopaque (IMPLANON)
  - The location noted when the implant was originally inserted
- If the implant is not palpable after insertion, check the applicator. The needle should be fully retracted and only the purple tip of the obturator should be visible. Confirm its presence in the arm with imaging techniques (X-ray, CT, USS, MRI) as soon as possible. The patient must use a back-up method of contraception until the presence of IMPLANON NXT has been confirmed.
- If these imaging methods fail to locate the implant, etonogestrel blood level determination can be used for verification of the presence of the implant. Please contact your local supplier for further guidance.
- IMPLANON NXT is radiopaque and is visible on X-rays and CT images as well as via MRI or ultrasound imaging techniques.
- NOTE: IMPLANON is not radiopaque and is not visible on X-ray or CT images. Attempts to localize a nonradiopaque implant via X-ray or CT will not be successful.
- USS characteristics of IMPLANON NXT:
  - Sharp acoustic shadow below the implant in the transverse position
  - Implant is a small echogenic spot (2 mm) when viewed in the transverse position
- MRI – Implant appears as a round hypodense area of 2-mm diameter, over a length of 4 cm. It is especially important to differentiate the implant from blood vessels.
- X-Ray – The implant will be visible as a 4-cm long, 2-mm wide white stick.
- CT scan – The implant will be visible as a round 2-mm wide radiopaque spot over a length of 4 cm.

Removing IMPLANON NXT™

- Indications for removal
  - Patient request
  - Medical indication
  - At the end of 3 years of use
- If the patient does not wish to become pregnant, another contraceptive method should be started immediately (return to normal menstrual cycle may be very rapid).
- Before initiating the removal procedure, consult the User Card for the location of the implant. Verify the exact location of the implant in the arm by palpation.

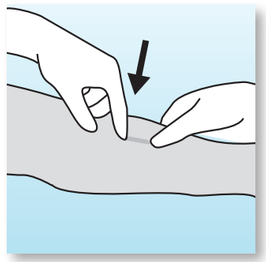
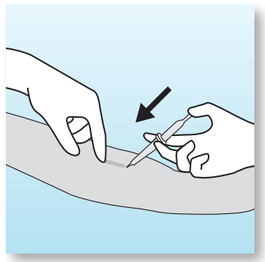


Figure A



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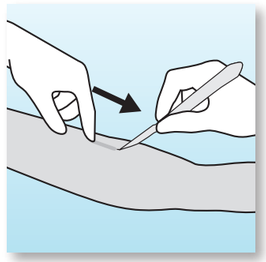

Figure C

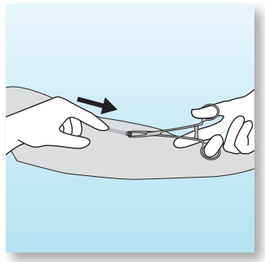

Figure D

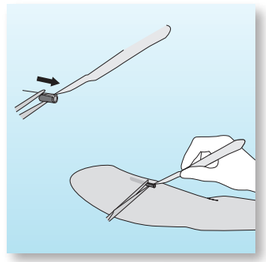

Figure E

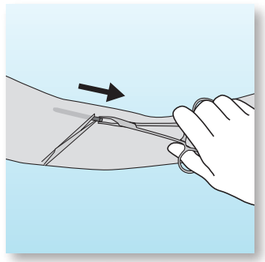

Figure F

- If the implant is not palpable, 2-dimensional X-ray can be performed to verify its presence. A non-palpable implant should always be first located prior to removal. Suitable methods for localization include X-ray computer tomography (CT), ultrasound scanning (USS) with a high-frequency linear array transducer (10 MHZ or greater), or magnetic resonance imaging (MRI). If these imaging methods fail to locate the implant, etonogestrel determination can be used for verification of the presence of the implant. Please contact your local supplier for further guidance.
- After localization of a non-palpable implant, consider conducting removal with ultrasound guidance.
- There have been occasional reports of migration of the implant; usually this involves minor movement relative to the original position unless inserted too deeply. This may complicate localization of the implant by palpation, USS, and/or MRI, and removal may require a larger incision and more time.
- Removal of IMPLANON NXT should be performed under aseptic conditions and **only** by a health care provider who is familiar with the removal technique.
- **Exploratory surgery without knowledge of the exact localization of the implant is strictly discouraged.**
- Removal of deeply inserted implants should be conducted with caution in order to prevent damage to deeper neural or vascular structures in the arm and should be performed only by health care providers familiar with the anatomy of the arm.
- If the implant cannot be removed, please contact your local supplier for further guidance.
- Clean the site where the incision will be made and apply an antiseptic. Locate the implant by palpation and mark the distal end (end closest to the elbow), for example, with a sterile marker (Figure A).
- Anesthetize the arm, for example, with 0.5 to 1 mL 1% lidocaine at the marked site where the incision will be made (Figure B). Be sure to inject the local anesthetic under the implant to keep it close to the skin surface.
- Push down the proximal end of the implant (Figure C) to stabilize it; a bulge may appear indicating the distal end of implant. Starting at the distal tip of the implant, make a longitudinal incision of 2 mm toward the elbow.
- Gently push the implant towards the incision until the tip is visible. Grasp the implant with forceps (preferably curved mosquito forceps) and remove the implant (Figure D).
- If the implant is encapsulated, make an incision into the tissue sheath and then remove the implant with forceps. (Figures E and F).
- If the tip of the implant does not become visible in the incision, gently insert a forceps into the incision (Figure G). Flip the forceps over into your other hand (Figure H). With a second pair of forceps carefully dissect the tissue around the implant and grasp the implant (Figure I). The implant can then be removed.
- Confirm that the entire rod, which is 4 cm long, has been removed by measuring its length.
- There have been occasional reports of migration of the implant. This may complicate localization of the implant by palpation, USS, and/or MRI, and removal may require a larger incision and more time.
- If the woman would like to continue using IMPLANON NXT, a new implant may be inserted immediately after the old implant is removed (see "How to Replace IMPLANON NXT")
- Close the incision with a steri-strip and apply an adhesive bandage.
- Apply sterile gauze with a pressure bandage to minimize bruising.
- If the woman does not wish to continue using IMPLANON NXT and does not want to become pregnant, another contraceptive method should be recommended.

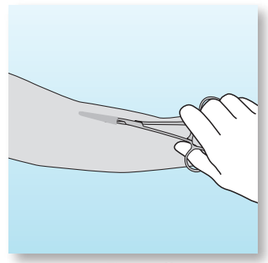

Figure G

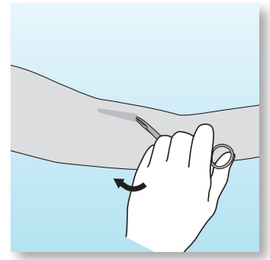

Figure H

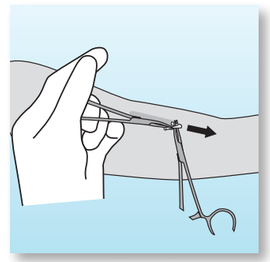

Figure I

How to Replace IMPLANON NXT

- Immediate replacement can be done after removal of the previous implant and is similar to the insertion procedure described in the section "How to Insert Implanon NXT."
- The new implant may be inserted in the same arm, and through the same incision from which the previous implant was removed. If the same incision is being used to insert a new implant, anesthetize the insertion site (eg, 2 mL lidocaine [1%]) applied just under the skin commencing at the removal incision along the insertion canal. Then follow the subsequent steps in the insertion instructions.

Before administering IMPLANON NXT, please read the Prescribing Information.

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