Implantable Contraceptives

Procedure Day
Fridays at the University

Dr. Kelby Cleverley, March 2024

Presenter Disclosure

Dr. Kelby Cleverley

- No financial relationship with Organon
- Honoraria from the University of Manitoba for this talk

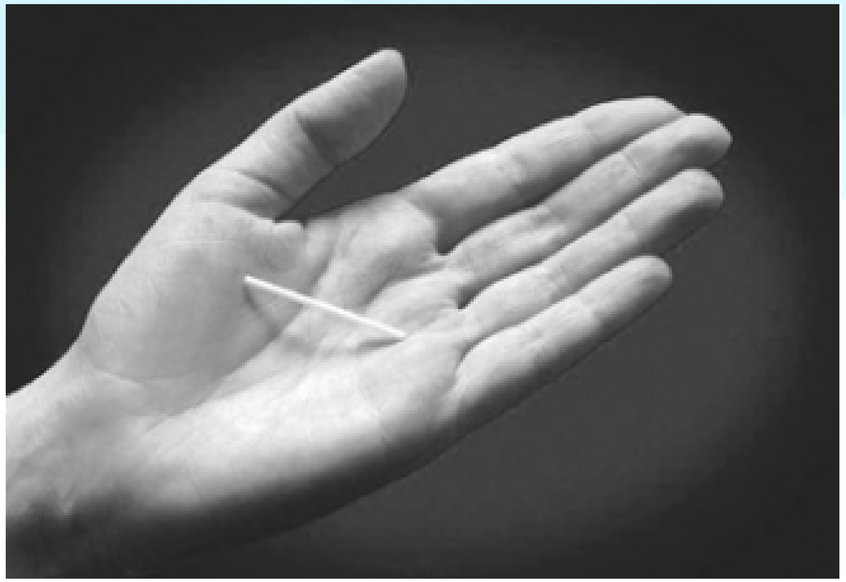
Learning Objectives

- Briefly discuss mechanism of action, pharmacokinetics and efficacy
- Review the risks and benefits of etonogesterel extended release subdermal implant, contraindications and other considerations
- Review key patient counselling topics
- Review the insertion and removal of the implant
- Trouble shooting tips
- Clinical case

Etonogestrel Subdermal Implant

What is it?

- Approved for use by Health Canada in May 2020
- Use in the US started in 2006
- Is approved for use in >100 countries, first used in Indonesia in 1998
- Has changed the contraceptive landscape in Canada as it provides another option for long acting reversible contraceptive (LARC) and does not require uterine placement



Etonogestrel Subdermal Implant

What is it?

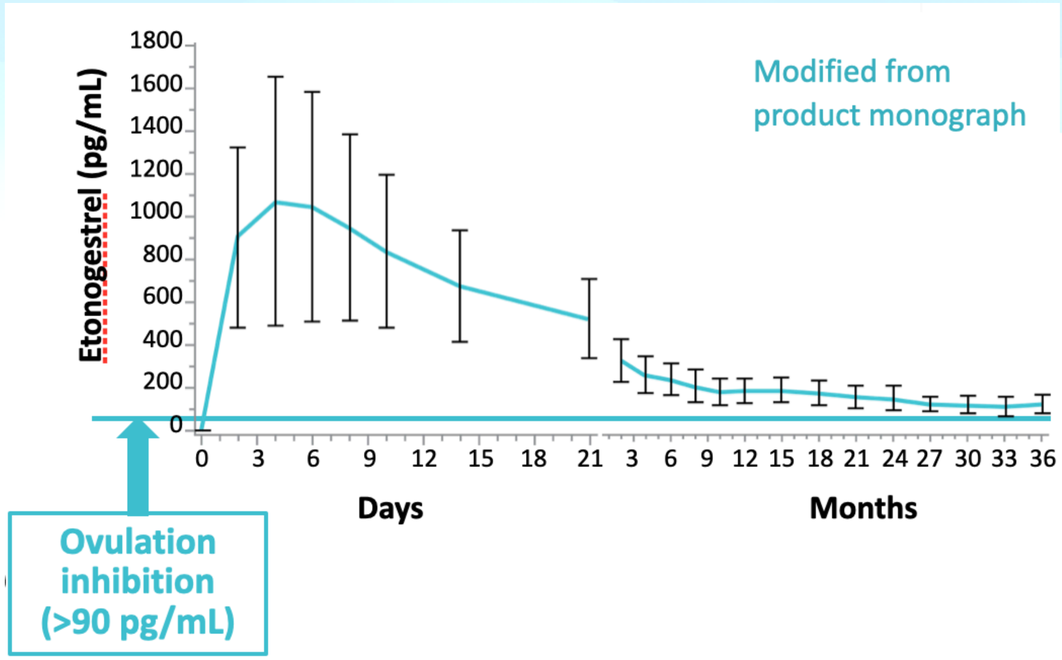
- Single flexible rod
  - 4cm long, 2mm wide
- Comes preloaded in a sterile disposable applicator
- Progestin only
  - Etonogestrel is the active metabolite of desogestrel
- Radiopaque (change from Implanon)
- Effective for contraception for 3 years

Nexplanon (etonogestrel extended release subdermal implant) product monograph. Kirkland, QC: Organon Canada Inc.
Rowlands S, Searle S. *Open Access Journal of Contraception* 2014;5:73-84.

Etonogestrel Subdermal Implant

Mechanism of Action & Pharmacokinetics

- Works primarily by inhibiting ovulation
- 68mg of etonogestrel per implant and delivers up to 70mcg etonogestrel per day (1)
- >90pg/mL required to inhibit ovulation, this is reached within one day (2)
- Maximum concentration occurs within 2 weeks (1200pg/mL) (1)



1. Nexplanon (etonogestrel extended release subdermal implant) product monograph. Kirkland, QC.
2. Palomba S et al. *Gynecol Endocrinol* 2012;28:710-21.

Etonogestrel Subdermal Implant

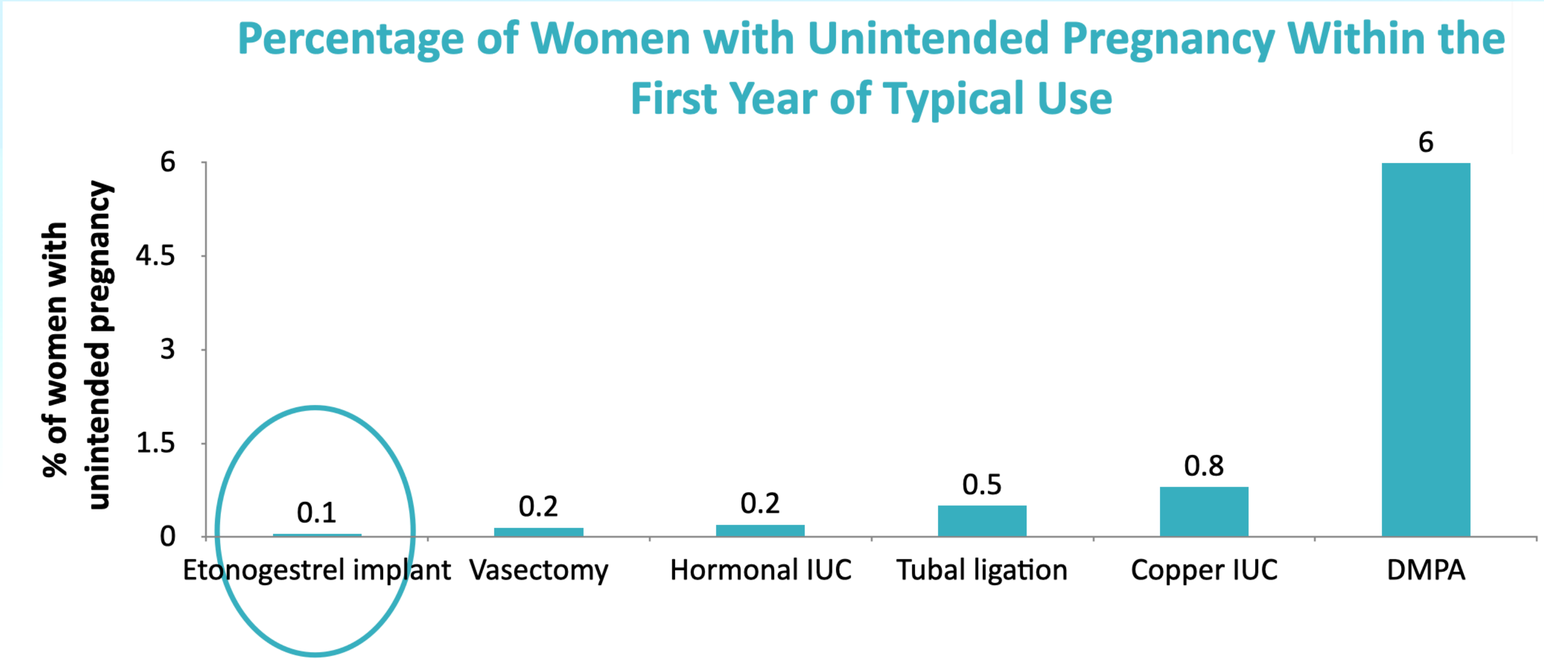
Mechanism of Action & Pharmacokinetics

- After implant removal, etonogestrel levels drop rapidly to undetectable levels within 1 week
- Pregnancies reported as soon as 7-14 days after removal
- Ovulation resumes within 2-4 weeks for most women
- Not studied in women >130% of their ideal body mass

Etonogestrel Subdermal Implant

Efficacy

- No pregnancies in clinical trials of up to 3 years duration*
- 923 subjects in 11 studies (ages 18-40 years)



*Based on data from clinical trials with Implanon (non-radiopaque etonogestrel subdermal implant); women weighing more than 130% of their ideal body weight or taking chronic medications that induce liver enzymes were excluded

CI, confidence interval

Nexplanon (etonogestrel extended release subdermal implant) product monograph. Kirkland, QC.

Etonogestrel Subdermal Implant

Adverse Effects & Risks

Adverse event	% of patients N = 942
Headache	15.5%
Weight increase	12.0%
Acne	11.8%
Breast pain	10.2%
Emotional lability	5.8%
Abdominal pain	5.2%

Reason for discontinuation	% of all patients (N=942)
Bleeding irregularities*	10.4%
Planning pregnancy	4.1%
Other reasons	3.5%
Lost to follow-up	2.4%
Amenorrhoea	0.7%

Reason for discontinuation	% of all patients (N=942)
Any adverse event	13.9%
Emotional lability	2.3%
Weight increase	2.3%
Headache	1.6%
Acne	1.3%
Depression	1.0%

*Bleeding irregularities were excluded from adverse event analyses because they are an expected adverse effect of progestin-only contraceptives

Blumenthal PD et al. *Eur J Contracept Reprod Health Care* 2008;13(Suppl 1):29–36.

Etonogestrel Subdermal Implant

Adverse Events & Risks: Insertion & Removal Complications

- Implant site reactions reported in 8.6% of patients including: erythema (3.3%), hematoma (3.0%), bruising (2.0%), pain (1.0%) and swelling (0.7%)
- Deep or incorrect insertions have been associated with paresthesia, migration and in rare cases intravascular insertion
- Incomplete insertion
- In rare post-marketing reports, implants were reported to have located within the vessels of the arm and the pulmonary artery
- There have been reports of broken or bent implants

Etonogestrel Subdermal Implant

Adverse Events and Risks: Potential Drug Interactions

- Anticonvulsants (carbamazepine, phenytoin, topiramate)
- Antimicrobials (rifampicin)
- HIV medications (Efavirenz, (fos)amprenavir, nelfinavir, nevirapine, tipranavir; ritonavir alone or in combination with darunavir, (fos)amprenavir, lopinavir, saquinavir, tipranavir)
- St. Johns Wort
- Bosentan
- Aprepitant (chemo-induced nausea)

Nexplanon (etonogestrel extended release subdermal implant) product monograph. Kirkland, QC: Organon Canada Inc; October 12, 2022.; Curtis KM et al. *MMWR Recomm Rep* 2016;65:1-66.

Etonogestrel Subdermal Implant

Contraindications

Product monograph[1]	CDC SPR[2] and SOGC[3] MEC 3/ 4
Progestin-only contraceptives should not be used in the presence of any of the conditions listed below. If the conditions appear during use, the product should be stopped immediately. • Known or suspected pregnancy • Known or suspected breast cancer • Personal history of breast cancer or other progestin-sensitive cancer, now or in the past • Liver tumors, benign or malignant, or active liver disease • Undiagnosed abnormal genital bleeding • Current or past history of thrombosis or thromboembolic disorders	MEC 4 • Current breast cancer (within 5 years) MEC 3 • Past breast cancer and no evidence of current disease for 5 years • Liver tumors: malignant tumors, hepatocellular adenoma • Severe (decompensated) cirrhosis • Unexplained vaginal bleeding • SLE with positive or unknown antiphospholipid antibodies

CDC SPR, Centers for Disease Control and Prevention selected practice recommendations; MEC, medical eligibility criteria.
SOGC, Society of Obstetricians and Gynaecologists of Canada
Nexplanon (etonogestrel extended release subdermal implant) product monograph. Kirkland, QC: Organon Canada Inc.
Curtis KM et al. *MMWR Recomm Rep* 2016;65:1-66; 3. Black A et al. *J Obstet Gynaecol Can* 2016;38:279-300.

Etonogestrel Subdermal Implant

Key Counselling Topics: Insertion Timing

Clinical Scenario	Product monograph Recommendations[1]	CDC [2] and SOGC Recommendations[3]
No HC use in past month	Between Day 1 to Day 5 of the menstrual cycle	• Can be inserted **at any time** if it is reasonably certain the woman is not pregnant • If inserted at any time other than Days 1 to 5, utilize **back-up contraception** and/or overlap for 7 days • If switching from IUC, back-up contraception recommended for 7 days after insertion or IUC can be removed ≥ 7 days after implant insertion
Switching from combined oral contraceptive pill (COC)	Day after last active tablet At latest, day following tablet-free or placebo tablet	
Switching from combined hormonal contraceptive patch or vaginal ring	Day of removal At latest, day of next application	
Switching from progestin-only pills	Any day of the month (within 24 hours of last pill)	
Switching from progestin-only injection, implant, or IUS	Same day injection is due or previous implant/IUS removed	

- General safe guidance is use back up contraceptive for 7 days with any contraceptive method

CDC SPR, Centers for Disease Control and Prevention; HC, hormonal contraceptive; IUC, intrauterine contraceptive; SOGC, Society of Obstetricians and Gynaecologists of Canada

1. Nexplanon (etonogestrel extended release subdermal implant) product monograph. Kirkland, QC: Organon Canada Inc.;
2. Curtis KM et al. *MMWR Recomm Rep* 2016;65:1-66;
3. Black A et al. *J Obstet Gynaecol Can* 2016;38:279-300.

Etonogestrel Subdermal Implant

Key Counselling Topics: Bleeding

Etonogestrel subdermal implant bleeding patterns during the first 2 years of use*

Bleeding pattern	Definition	% of 90-day intervals with this pattern
Amenorrhea	No bleeding or spotting	22.2%
Infrequent	<3 bleeding/spotting episodes in 90 days (excluding amenorrhea)	33.6%
Frequent	More than 5 bleeding/spotting episodes	6.7%
Prolonged	Any bleeding/spotting episode > 14 days	17.7%

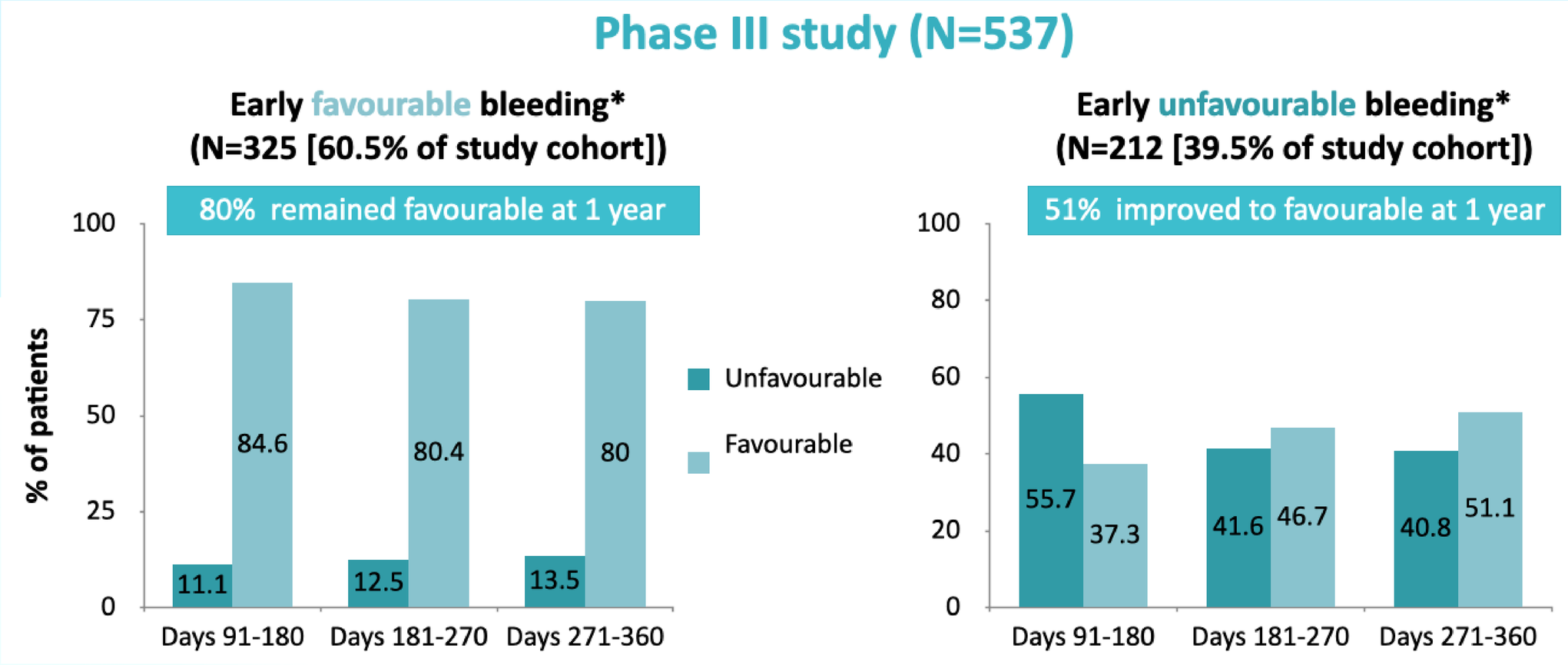
Over half of women have no bleeding or infrequent bleeding

*Based on 3315 recording periods of 90 days duration in 780 women, excluding the first 90 days after implant insertion

Nexplanon (etonogestrel extended release subdermal implant) product monograph. Kirkland, QC: Organon Canada Inc.

Etonogestrel Subdermal Implant

Key Counselling Topics: Bleeding



Mansour D, Fraser IS, Edelman A, et al. Can initial vaginal bleeding patterns in etonogestrel implant users predict subsequent bleeding in the first 2 years of use? *Contraception* 2019;100:264-8.

Etonogestrel Subdermal Implant

Key Counselling Topics: Dysmenorrhea

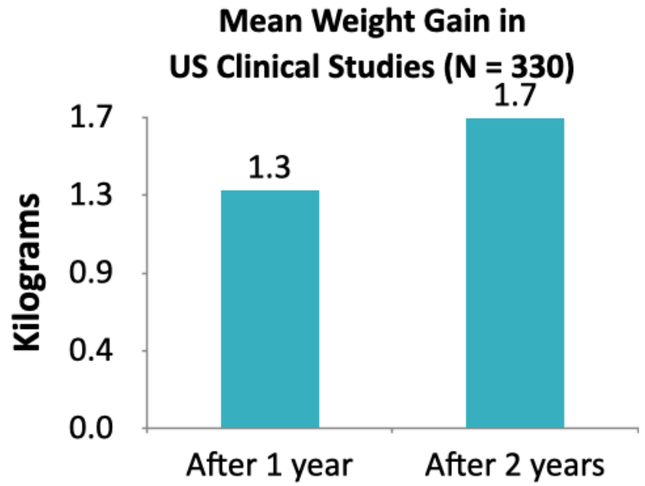
- Dysmenorrhea generally improves during implant use
- A open label clinic study of 647 patients found that of those who at baseline had dysmenorrhea (315 patients), 77% reported symptom resolution at the time of implant removal
- 13% had no change in their symptoms and 4% reported increased severity
- Of those reporting no dysmenorrhea at baseline (332 patients), 93% reported no change at removal of the implant, 7% reported an increase in dysmorrhea

Mansour D et al. *Eur J Contracept Reprod Health Care* 2008;13(suppl 1):13–28.

Etonogestrel Subdermal Implant

Key Counselling Topics: Weight Gain

Clinical Trials in Women 18 to 40 Years (No Control Group)[1]



- **Extent of weight gain related to the implant is unknown**

Single-center Study in Adolescents (Control Group)[2]

- Etonogestrel subdermal implant users compared with controls (hormonal pills, patch, or ring; former/current DMPA use excluded)
  - Matched for age, BMI, and race
  - 197 females in each group
  - Mean age 17 years
  - Mean implant use 24.5 months
- **Weight gain was similar for implant users and controls (3.6 vs 3.1 kg); *P* =0.43**

BMI, body mass index; DMPA, depot medroxyprogesterone acetate

1. Nexplanon (etonogestrel extended release subdermal implant) product monograph. Kirkland, QC: Organon Canada Inc.
2. Romano ME, Braun-Courville DK. *J Pediatr Adolesc Gynecol* 2019;32:409-14.

Etonogestrel Subdermal Implant

Pregnancy and Breast/Chest feeding

- If pregnancy occurs while implant present
  - Implant should be removed
  - Will not provoke pregnancy loss
  - Is not associated with birth defects
- Small amount of etonogestrel is excreted in the breast milk
- Risk of progestin only options on breastfeeding is theoretical
  - Recommend using caution in a lactating patient who has existing supply concerns or other lactation risk factors

Etonogestrel Subnormal Implant

Key Counselling Topics: STIs

Always remind patients that the implant does not prevent or protect against sexually transmitted infections!

Photo: https://fpt.org.au/advice-and-information/contraception/barrier-protection/

Etonogestrel Subdermal Implant

Insertion

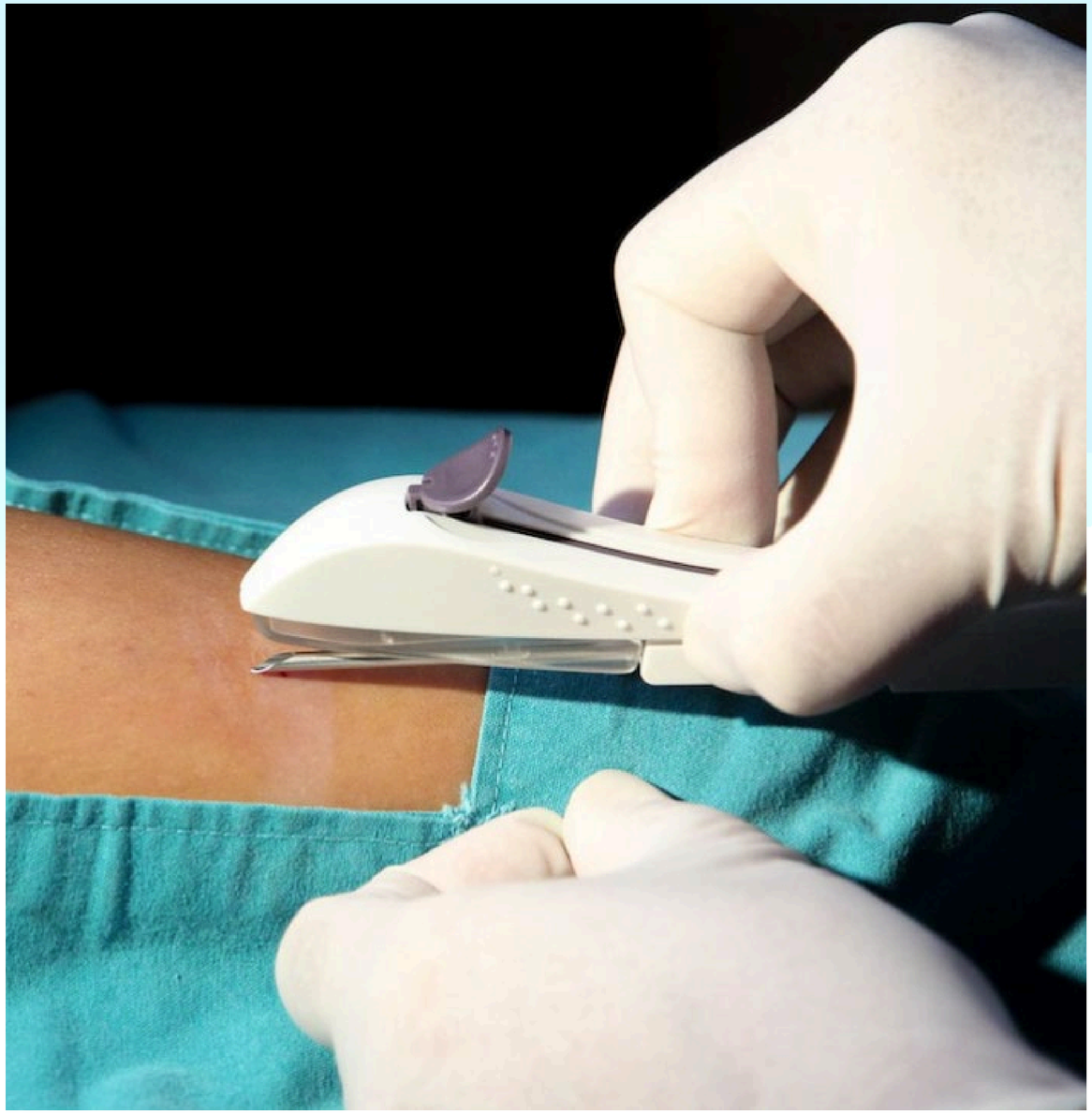
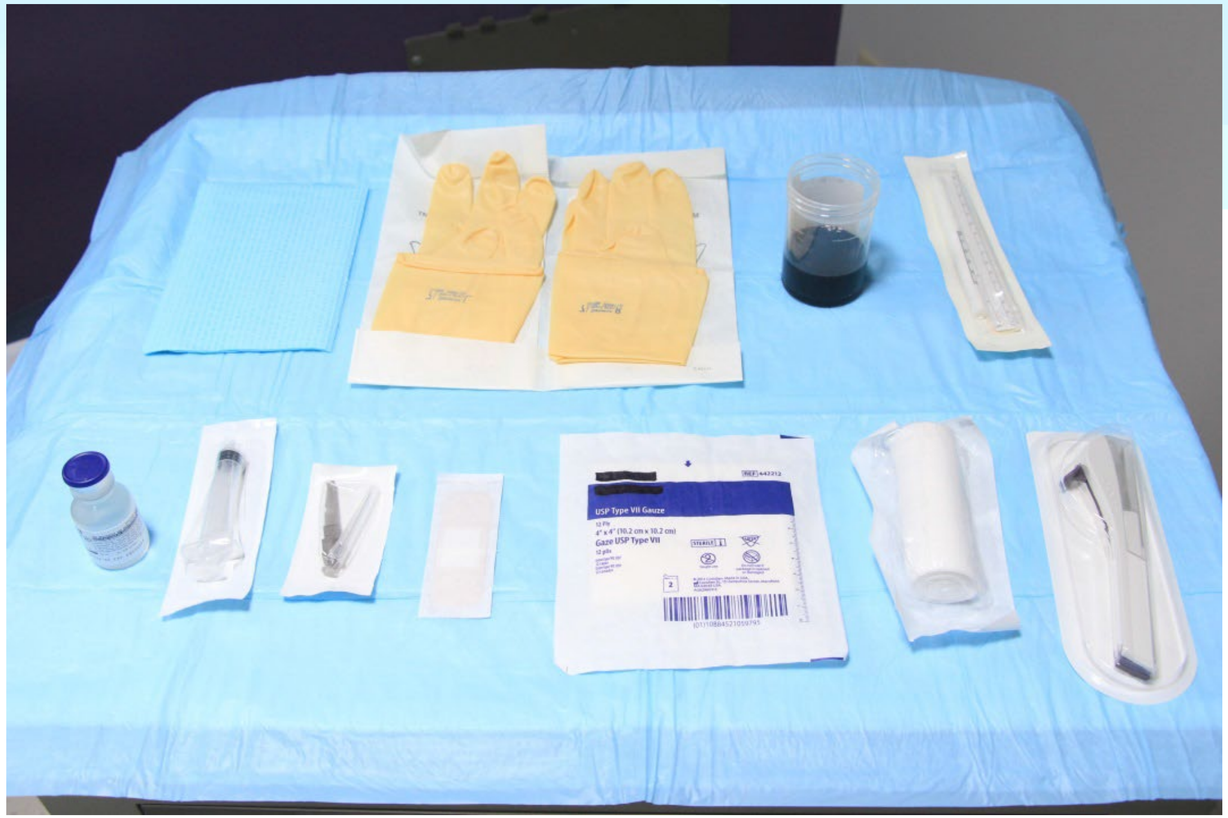


Photo: https://obgynmiami.com/blog/nexplanon-vs-implanon/

Etonogestrel Subdermal Implant

Insertion

- What you will need:
  - Patient positioned properly
  - Etonogestrel Subdermal Implant with applicator
  - Skin marker & ruler
  - Sterile gloves & drape
  - Cleaning solution
  - Local anesthetic & needle
  - Sterile gauze
  - Adhesive bandage
  - Pressure bandage



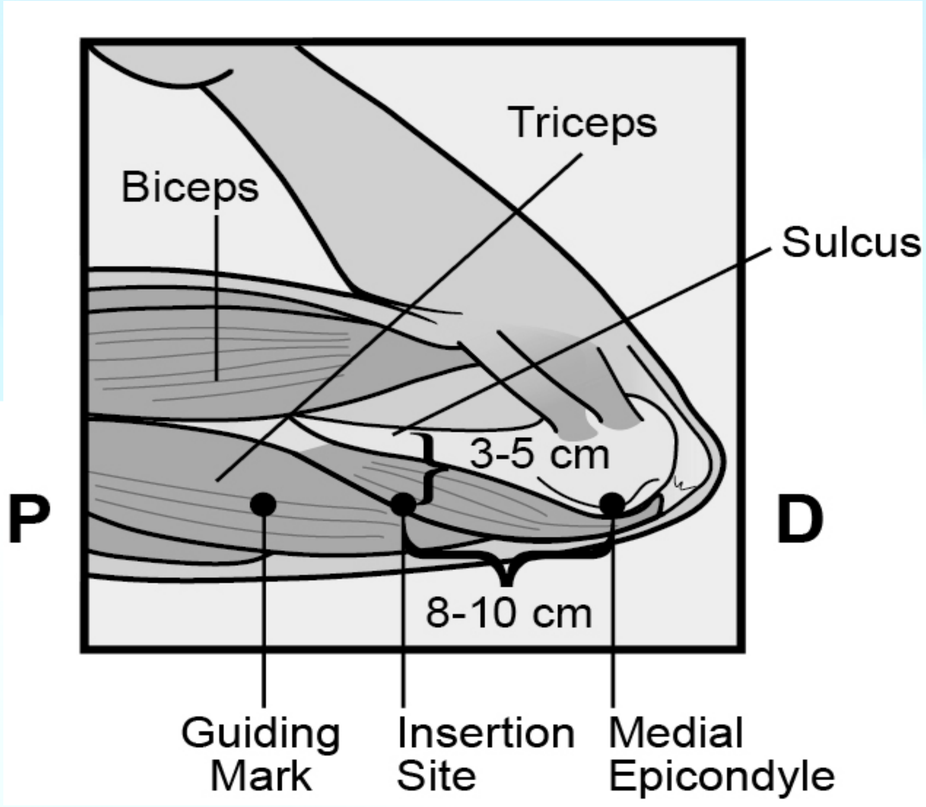
Etonogestrel Subdermal Implant

Insertion

- Have patient lay on their back with non-dominant arm flexed at the elbow and externally rotated with the hand underneath their head
- This position helps to deflect the ulnar nerve from the insertion site
- You want to be able to see the advancement of the needle/applicator from the side view to ensure it is superficial and completely inserted

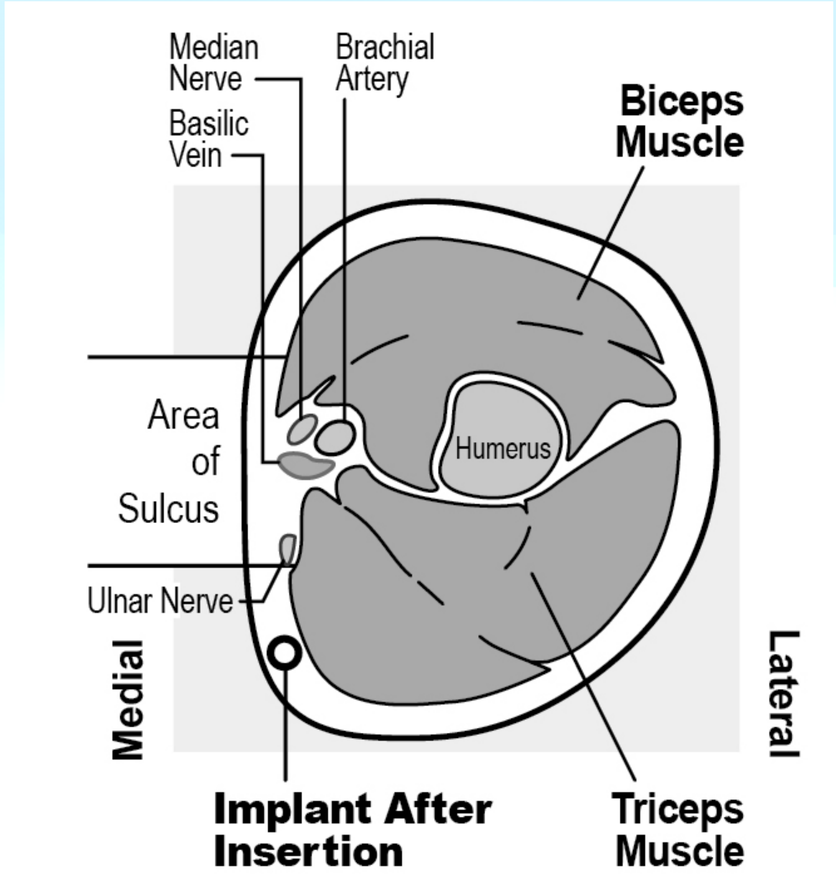
Etonogestrel Subdermal Implant

Insertion - Landmarking



For illustrative purposes, figures depict the left inner arm

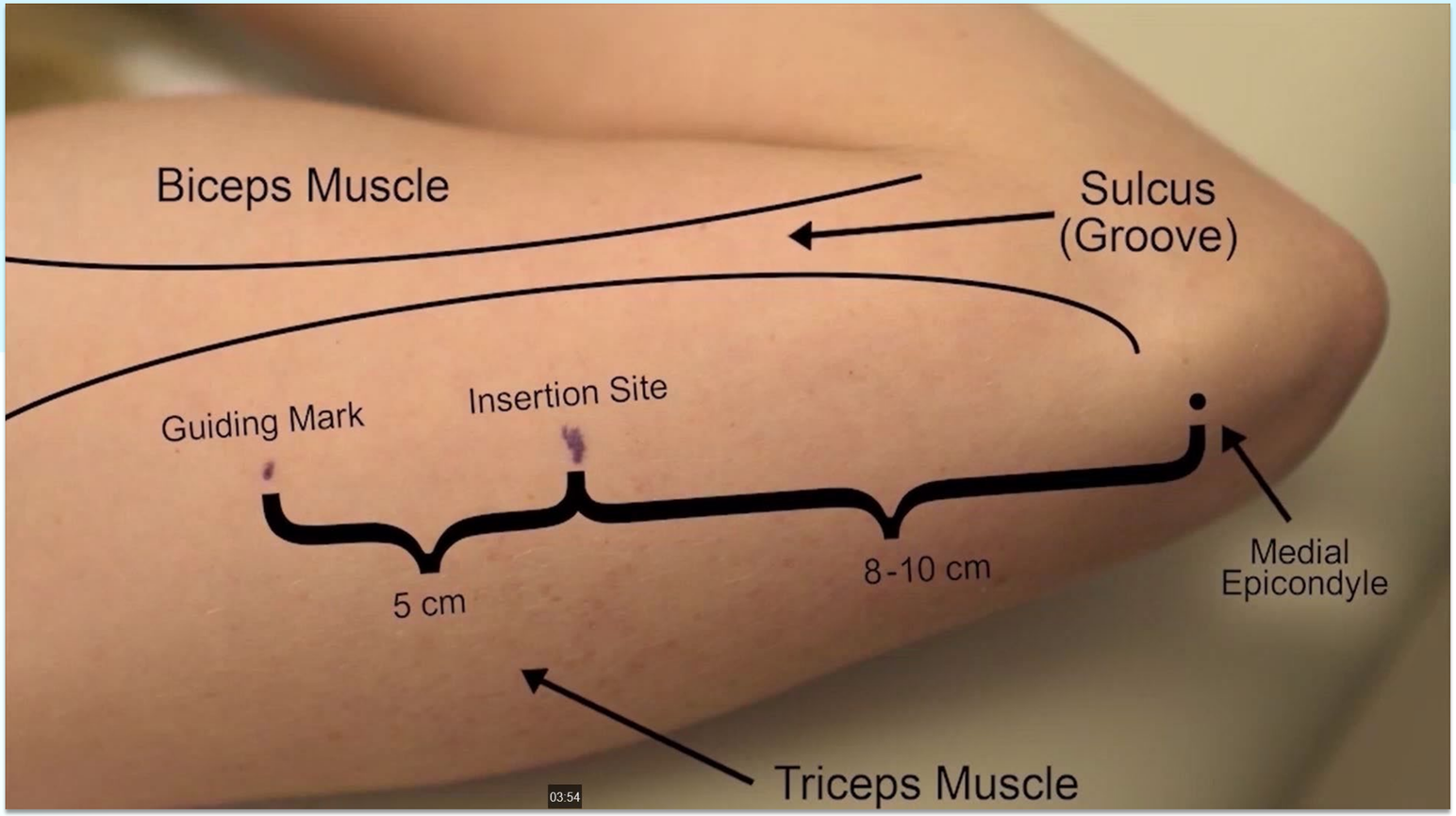
P – proximal (toward the shoulder)
D – distal (toward the elbow)



Cross section of the upper left arm, as viewed from the elbow

Etonogestrel Subdermal Implant

Insertion



Etonogestrel Subdermal Implant

Insertion

- Once landmarked you will clean the skin then infiltrate the *entire course* of the implant with local anaesthetic
- Cleanse the skin again and drape the area desired
- Check that the area is adequately anesthetized
- Visually inspect Nexplanon inserter, hold applicator at textured surface, retract the skin on the arm distally
- Insert needle at a 30 degree angle at your insertion mark until entire bevel is just under the skin
- Once the entire bevel is under the skin, drop the angle of the applicator so that it is horizontal and tent the skin as you progress the needle
- Ensure entire needle is entered into the skin prior to pressing purple slider - purple slider retracts the needle and if needle is not completely in the skin this will result in an incomplete insertion and will require a new implant
- Once the implant is inserted, cover the insertion site with an adhesive bandage
- Palpate the implant and then have the patient feel the implant as well
- Cover the area with a pressure bandage and advise them to leave this on for 24 hours, the bandaid should remain for 3-5 days

Etonogestrel Subdermal Implant

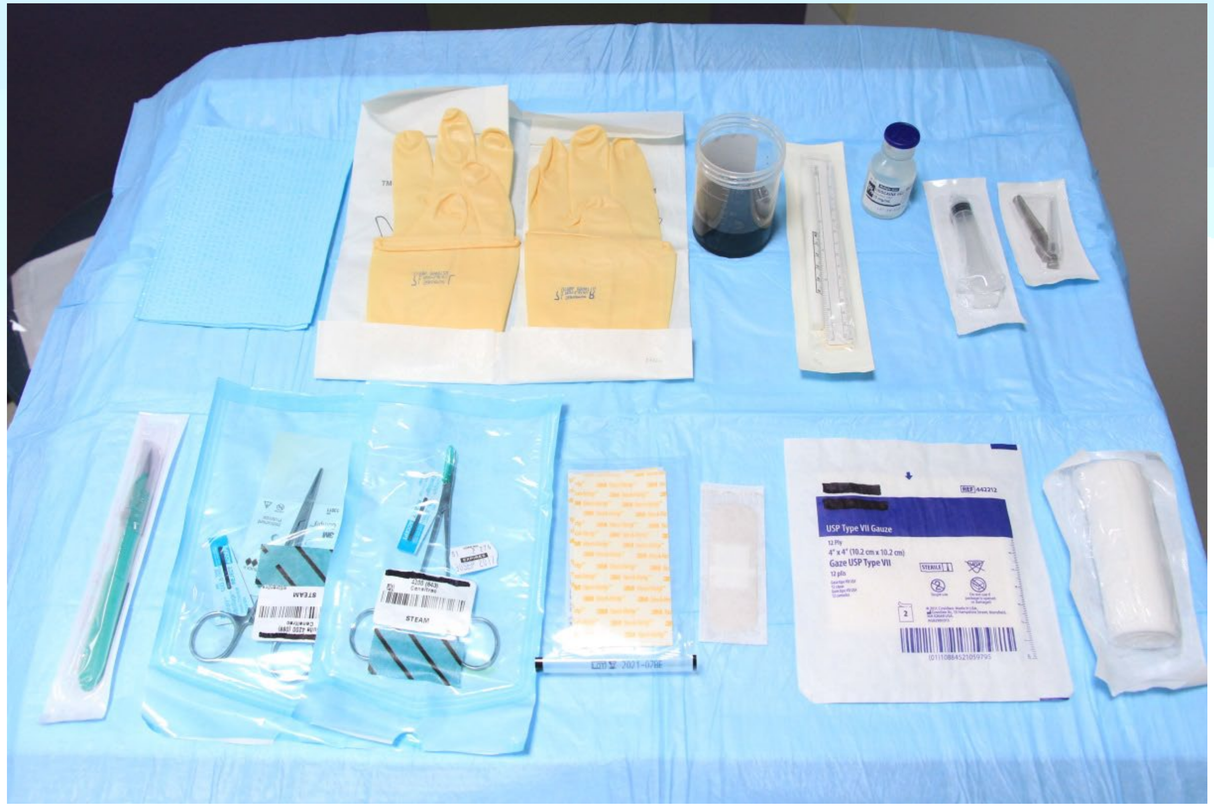
Insertion

(nexplanonvideos.com)

Etonogestrel Subdermal Implant

Removal

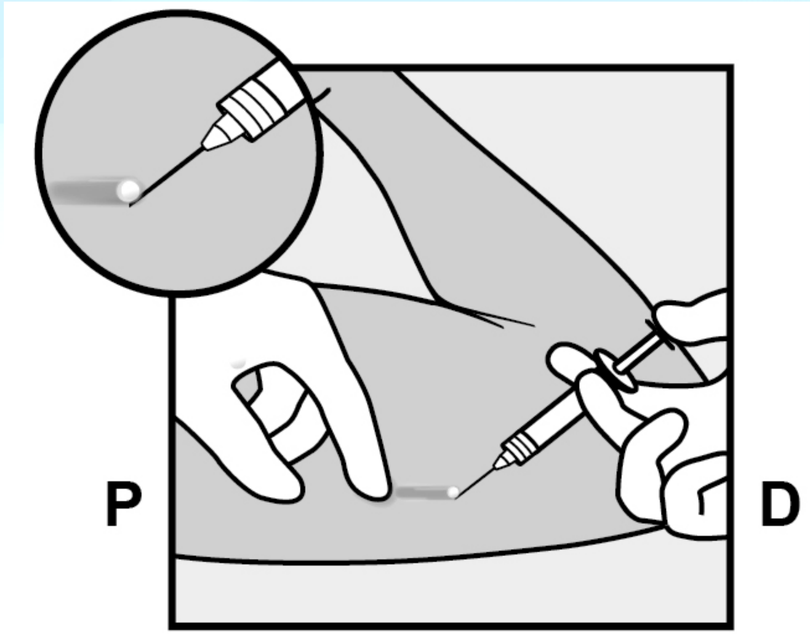
- You’ll need:
  - Sterile gloves
  - Cleaning solution
  - Skin marker
  - Anesthetic
  - Scalpel
  - Forceps
  - Gauze
  - Steristrip
  - Adhesive bandage
  - Pressure bandage



Etonogestrel Subdermal Implant

Removal

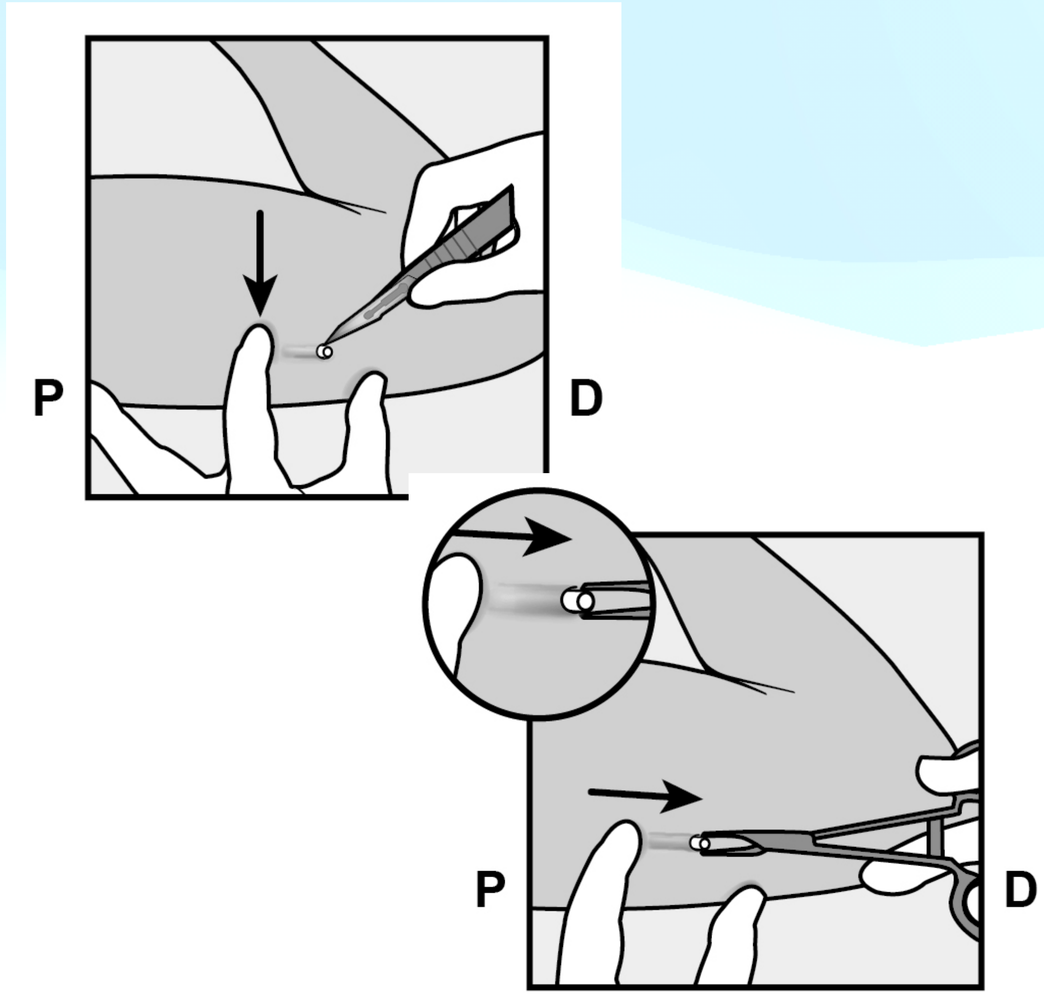
- Position the same way as for insertion
- Locate the implant by palpation, push down on the proximal end of the implant which should tent up the distal tip
- Mark the distal tip with a skin marker
- Clean the skin and then anesthetize the site where the incision will be made
- Place anesthetic below the tip of the implant to bring it close to the surface



Etonogestrel Subdermal Implant

Removal

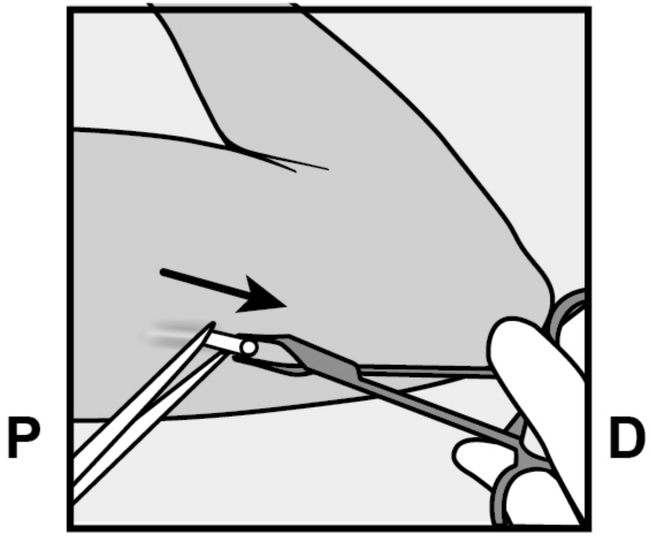
- Push down on the proximal end of the implant
- Make a small incision parallel with the implant just overlying the tip
- The tip of the implant may pop through the incision which can then be grasped with forceps a removed
- You may need to do some dissection of adherent tissue from the implant



Etonogestrel Subnormal Implant

Removal

- If the implant tip isn’t visible use small forceps to try to grasp the implant and then continue to grasp with another pair of forceps and direct adherent tissue as you go, you may need to make the incision slightly larger to accommodate the forceps
- If the implant cannot be grasped despite troubleshooting you can refer to a provider experienced with complex removals
- Organon Canada can connect you with a provider to help with difficult removals



Etonogestrel Subnormal Implant

Removal

- Ensure the entire implant is removed (measures 4cm in length)
- If you are replacing the implant is can be done in the same location through the same incision
- Cover the incision with a stern strip, adhesive bandage and then a pressure dressing (24 hours)
- The patient should immediately start another form of contraception if not planning pregnancy

Etonogestrel Subnormal Implant

Removal

(nexplanonvideos.com)

Etonogestrel Subdermal Implant

Clinical Case

- 23 year old female, G0
- Presenting for contraceptive counselling
- Has been using COC pill, interested in switching to LARC as forgetting to take pill
- PMHx: depression stable on SSRI
- No history of STI, dysmenorrhea or menorrhagia

Etonogestral Subnormal Implant

Case Continued

- Reviewed LARC options with patient
- She wished to avoid uterine placement
- Informed consent obtained
- Patient then returned for insertion
- Placed with no complications
- 4 week follow up arranged

Etonogestral Subnormal Implant

Case Continued

- At follow up patient reported prolonged bleeding since insertion
- Reports menses type bleeding
- Vitally stable, denies symptoms of anemia or hypovolemia
- Denies infectious symptoms, STBBI screening at time of insertion negative, patient denies new sexual contacts since that time
- Implant remains palpable

Etonorgestral Subnormal Implant

Case Continued

Therapy Regimen	Supporting Evidence
COC taken daily for 21 days followed by a 7-day break Use for up to 3 months	• Little supportive evidence • Anecdotally, appears to help in practice
High-dose cyclical progestin for up to 3 months (medroxyprogesterone acetate 10 mg twice daily or norethisterone 5 mg twice daily for 21 days with a 7-day break)	• No published evidence • Anecdotally, appears to help in practice
POP, particularly a desogestrel POP, daily for up to 3 months	• No published evidence • Anecdotally, may work in some cases
NSAIDs, especially COX-2 inhibitors, daily for 5-10 days	• Some published evidence • Anecdotally, may work in some cases
Tranexamic acid (500 mg) twice daily for 5 days	• Limited published evidence • Anecdotally, may work in practice

Mansour D, Bahamondes L, Critchley H et al, Contraception 83(2011)202-210

Etonogestral Subnormal Implant

Case Continued

- At follow up patient reported improved bleeding but still having irregular spotting
- Reviewed evidence of improvement in bleeding patterns in ~50% of people after one year
- Patient decided to watch and see

Etonogestral Subnormal Implant

Case Continued

- Patient returned at 12 month mark after insertion reporting ongoing unscheduled bothersome bleeding
- At that time STBBI testing repeated, bhcg negtive, implant palpable
- Reviewed options with patient again, this time opted for COC x 3 months (with withdrawal bleeds)
- At follow ups patient reported unscheduled bleeding had stopped with light regular menses

1. Nexplanon (etonogestrel extended release subdermal implant) product monograph. Kirkland, QC: Organon Canada Inc.

2. Romano ME, Braun-Courville DK. Assessing weight status in adolescent and young adult users of etonogestrel contracetive implant. *J Pediatr Adolesc Gynecol* 2019;32:409-14.

3. Mansour D, Fraser IS, Edelman A, et al. Can initial vaginal bleeding patterns in etonogestrel implant users predict subsequent bleeding in the first 2 years of use? *Contraception* 2019;100:264-8.

4. Palomba S et al. Nexplanon: the new implant for long-term contraception. A comprehensive descriptive review. *Gynecol Endocrinol* 2012;28:710-21.

5. Blumenthal PD et al. Tolerability and clinical safety of Implanon. *Eur J Contracept Reprod Health Care* 2008;13(Suppl 1):29–36.

6. Curtis KM et al. Removing medical barriers to contraception — evidence-based recommendations from the Centers for Disease Control and Prevention. *MMWR Recomm Rep* 2016;65:1-66; 3.

7. Black A et al. Canadian Contraception Consensus (Part 3 of 4): Chapter 8 - Progestin-Only Contraception. *J Obstet Gynaecol Can* 2016;38:279-300.