Insertion & Removal Procedures

Avibela®

(levonorgestrel-releasing intrauterine system) **52 mg**

INSERTION OF AVIBELA®

Planning for AVIBELA Insertion

- AVIBELA should only be inserted by a trained healthcare provider
- Be thoroughly familiar with the product, product educational materials, product insertion instructions, prescribing information, and patient labeling before attempting insertion of AVIBELA
- Obtain a complete medical & social history to determine conditions that might influence the selection of a levonorgestrel-releasing intrauterine system for contraception
- Exclude pregnancy and confirm that there are no contraindications to using AVIBELA
- Ensure that the woman understands the contents of the Patient Information Booklet and obtain consent
- Check the expiration date on the box before opening it. Do not insert AVIBELA after the expiration date

Note: The AVIBELA intrauterine system ("IUS") is also known as the hormonal intrauterine device ("IUD") and the levonorgestrel-releasing IUD

Timing of AVIBELA Insertion

Timing of AVIBELA insertion in women not currently using hormonal or intrauterine contraception

- AVIBELA can be inserted any time you can be reasonably certain the woman is not pregnant
  - Consider the possibility of ovulation and conception prior to initiation of this product
  - If AVIBELA is inserted after the first 7 days of the menstrual cycle, the patient should:
    - use a barrier method of contraception, or
    - abstain from vaginal intercourse

    for 7 days after insertion to prevent pregnancy

Timing of AVIBELA Insertion

Timing of AVIBELA insertion after first trimester abortion and miscarriage:

- **AVIBELA can be inserted immediately**

Timing of AVIBELA insertion after second trimester abortion and miscarriage or after childbirth:

- **After at least 4 weeks or until uterus is fully involuted**
  - If the woman has not yet had a period, consider the possibility of ovulation and conception occurring prior to insertion of AVIBELA
  - AVIBELA can be inserted any time the provider can be reasonably certain the woman is not pregnant
  - If AVIBELA is not inserted during the first 7 days of the menstrual cycle:
    - a barrier method of contraception should be used for 7 days, or
    - the patient should abstain from vaginal intercourse for 7 days
  - There appears to be an increased risk of perforation in lactating women

Timing of AVIBELA Insertion

Switching to AVIBELA from other contraceptives

Population	Insertion Timing Recommendations

Switching from oral, transdermal or vaginal hormonal contraceptive	• AVIBELA may be inserted at any time
	  • May be inserted during the hormone-free interval of the previous method
	  • If inserted during active use of the previous method, that method should be continued for 7 days after AVIBELA insertion or until the end of the current treatment cycle
	• If using continuous hormonal contraception, that method should be discontinued 7 days after AVIBELA insertion

Switching from injectable progestin contraceptive	• AVIBELA may be inserted at any time • If AVIBELA is inserted more than 3 months (13 weeks) after the last injection, a barrier method of contraception (such as condoms or spermicide) should also be used for 7 days after insertion
Switching from contraceptive implant or another IUS	• Insert AVIBELA on the same day the implant or IUS is removed • AVIBELA may be inserted at any time during the menstrual cycle

Items for Insertion

Additional items that may be useful could include:

- Local anesthesia, needle, and syringe
- Sterile os finder and/or cervical dilators
- Ultrasound with abdominal probe

Preparation for Insertion

- After opening the box, visually inspect the sealed pouch containing AVIBELA
  - Verify that it has not been damaged (e.g., torn, punctured, etc.)
  - If the packaging has any visual damage that could compromise sterility or performance, do not use the unit for insertion
- Complete the pelvic examination, speculum placement, tenaculum placement, and sounding of the uterus before opening the pouch
- Use aseptic technique during the entire insertion procedure
  - Loading and inserting AVIBELA does not require sterile gloves
  - If not using sterile gloves, complete all steps for loading the IUS (Steps 1-7) inside the pouch. Maintain sterility during insertion; do not touch AVIBELA or parts of any sterile instrument that will pierce tissue (e.g., a tenaculum on the cervix) or go into the uterine cavity

Preparation for Insertion

- Follow the insertion instructions exactly as described in order to ensure proper insertion
- Insertion may be associated with some pain and/or bleeding or vasovagal reactions (e.g., diaphoresis, syncope, bradycardia, or seizure), especially in patients with a predisposition to these conditions
  - Consider administering analgesics prior to insertion
- In case of difficult insertion and/or exceptional pain or bleeding during or after insertion, physical examination and ultrasound should be performed immediately to exclude perforation of the uterine body or cervix
  - If necessary, remove the system and insert a new, sterile system

Preparation for Insertion

- With the patient comfortably in lithotomy position, perform a bimanual exam to establish the size, shape, and position of the uterus and to evaluate any signs of uterine infection
- Gently insert a speculum to visualize the cervix
- Thoroughly cleanse the cervix and vagina with antiseptic solution
- Administer cervical anesthetic, if needed
- Apply a tenaculum to the cervix and use gentle traction to align the cervical canal with the uterine cavity
  - Keep the tenaculum in position and maintain gentle traction on the cervix throughout the insertion procedure

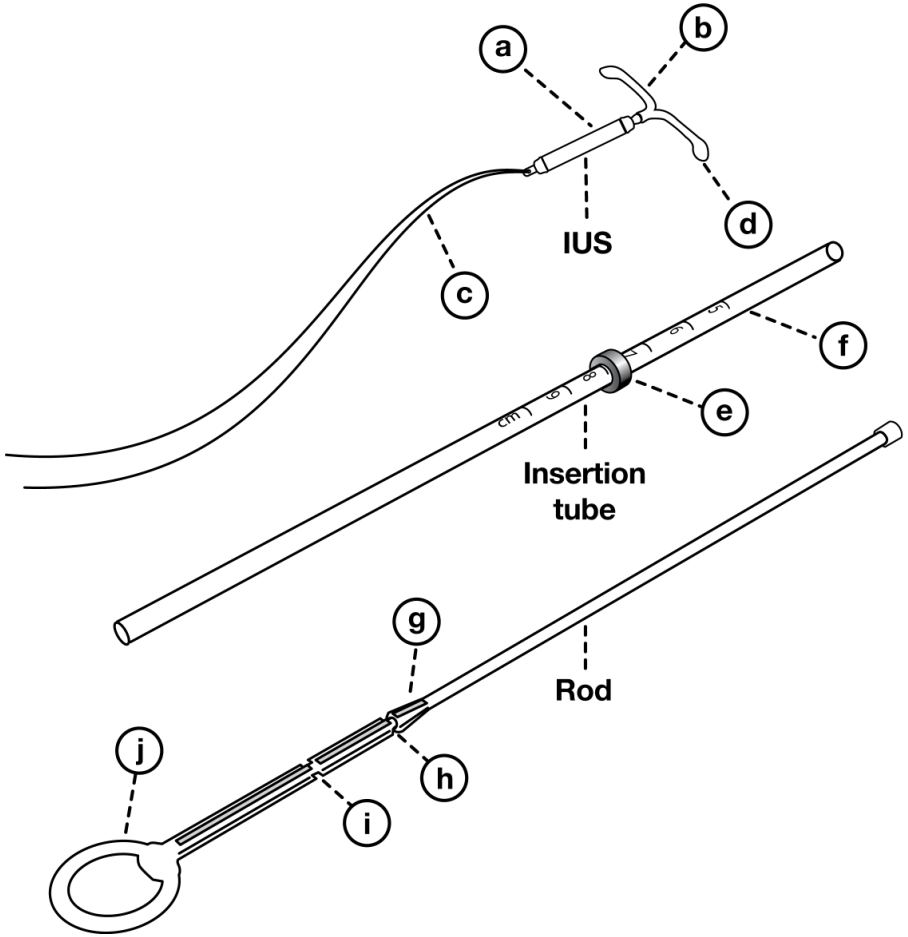
Sounding the Uterus

Carefully sound the uterus to measure its depth

- The uterus should sound to a depth of at least **5.5 cm**. Insertion of AVIBELA into a uterine cavity that sounds to less than 5.5 cm may increase the incidence of expulsion, bleeding, pain, perforation, and possibly pregnancy. AVIBELA should not be inserted if the uterus sounds to less than 5.5 cm
- Open the pouch containing AVIBELA only after ascertaining that the patient is appropriate for AVIBELA
- If you encounter cervical stenosis at any time during uterine sounding or AVIBELA insertion:
  - Use cervical dilators, not force, to overcome resistance
  - If necessary, dilation, sounding, and insertion may be performed with ultrasound guidance

AVIBELA Insertion Video

AVIBELA IUS and Inserter

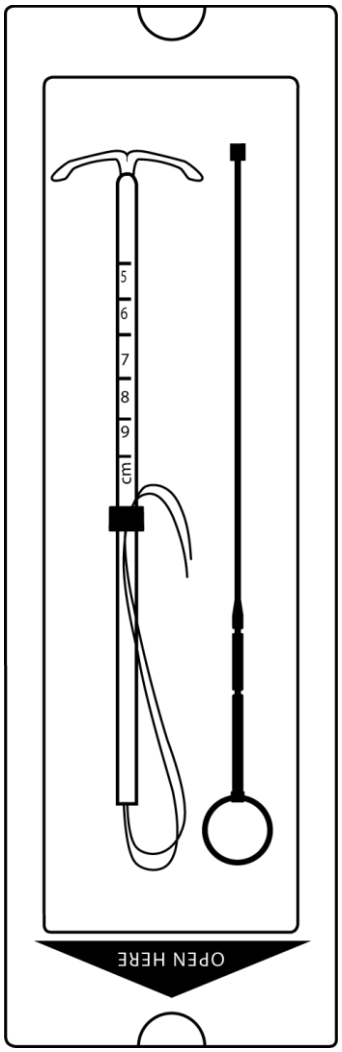


- (a) Levonorgestrel reservoir with membrane
- (b) Lateral arms
- (c) Blue removal threads
- (d) Knobs
- (e) Flange
- (f) Centimeter markings
- (g) Thickened mark
- (h) First indent
- (i) Second indent
- (j) Ring

Loading the IUS Into the Inserter

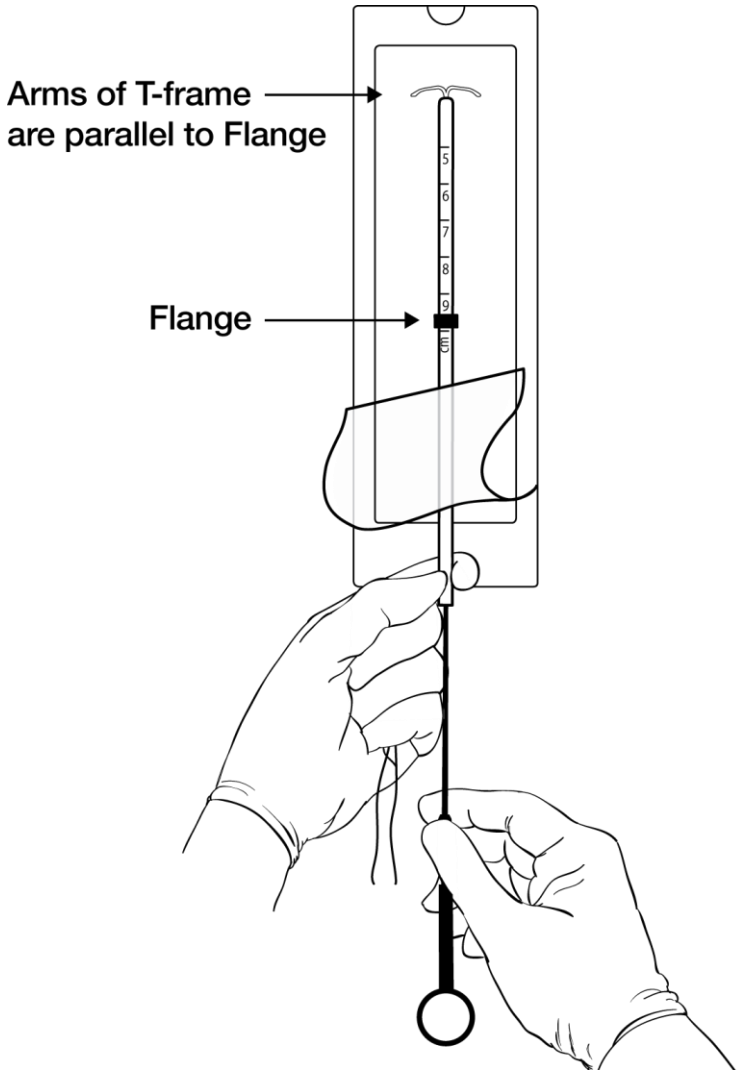
Step 1: Open the pouch

- Place the AVIBELA pouch on a flat surface with the clear side of the pouch facing up
- Open the sterile AVIBELA pouch from the bottom (end with the rod ring) approximately 1/3 of the way until the lower end of the IUS threads, the rod, and the insertion tube are exposed
- If using sterile gloves, you can open the pouch completely before putting on the sterile gloves



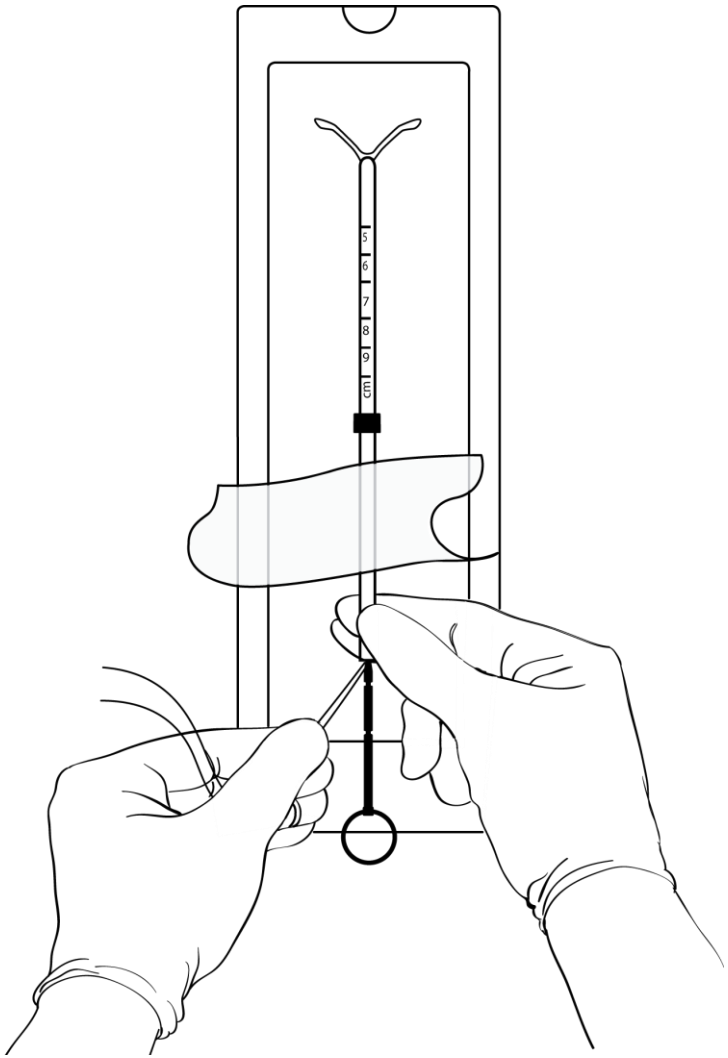
Loading the IUS Into the Inserter

Steps 2 and 3: Release the threads from the flange and insert the rod



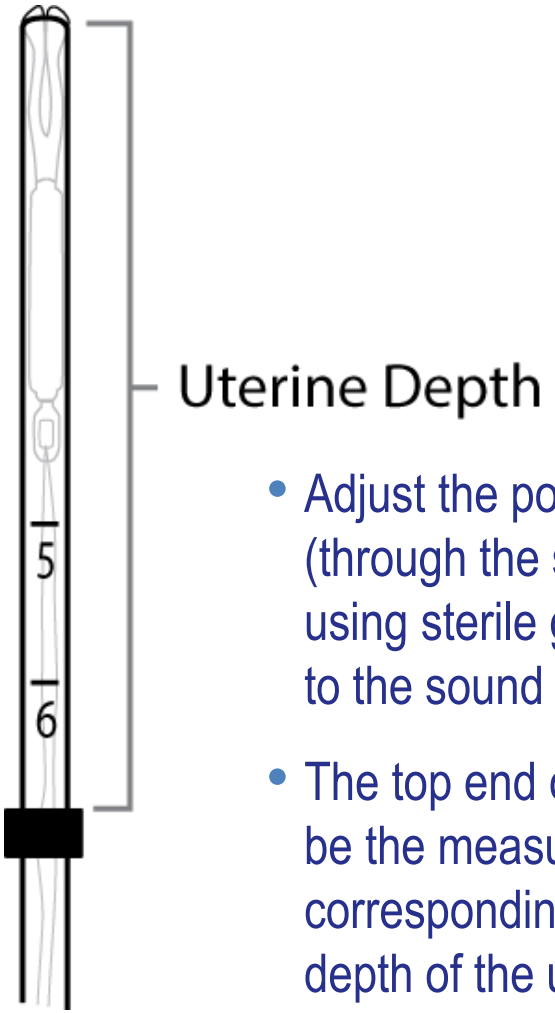
Loading the IUS Into the Inserter

Step 4: Draw the IUS into the insertion tube by pulling on the threads



Loading the IUS Into the Inserter

Step 5: Adjust the flange to the uterine depth



- Adjust the position of the flange (through the sterile package if not using sterile gloves) to correspond to the sound measurement
- The top end of the flange should be the measurement corresponding to the sounded depth of the uterus

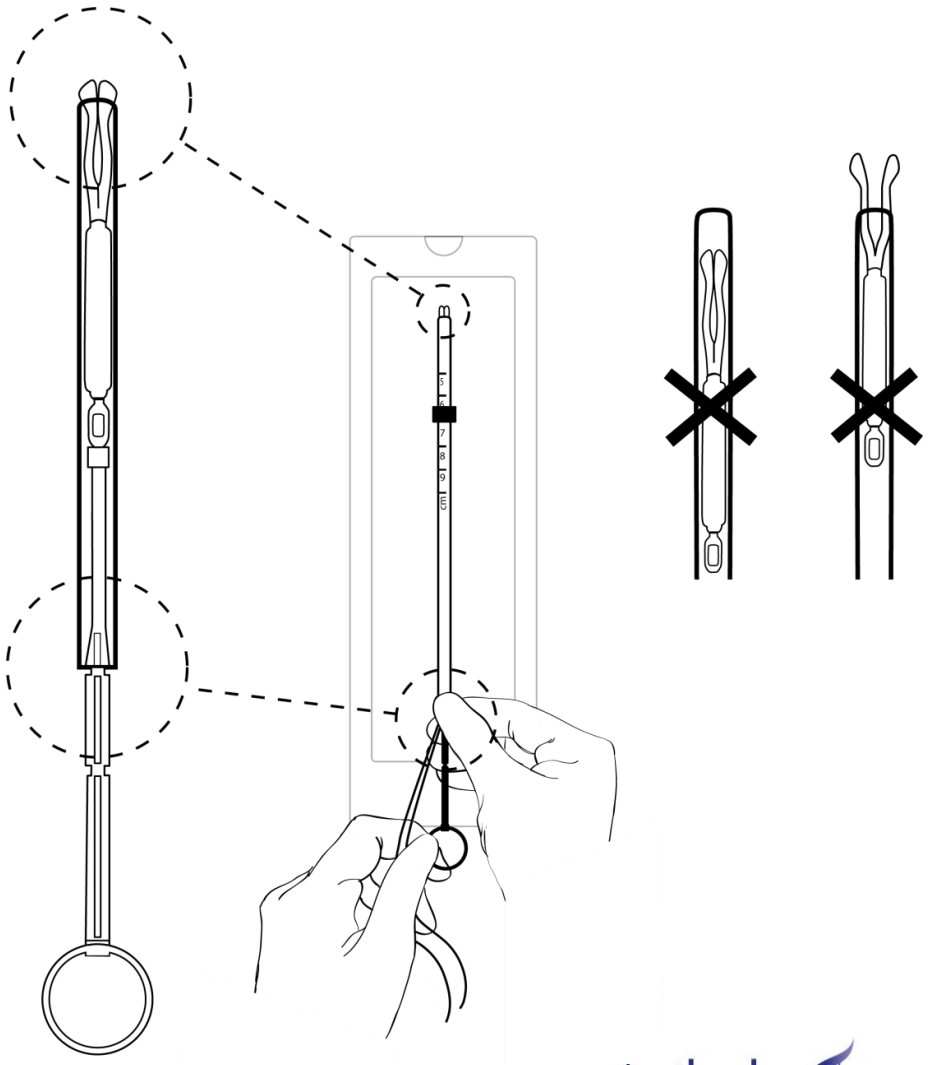
Loading the IUS Into the Inserter

Step 6: Final IUS positioning

ENSURE A HEMISPHERICAL DOME IS ACHIEVED

The hemispherical dome facilitates passage through the cervical os

- Position the IUS in the tube so that the knobs of the lateral arms form a hemispherical dome
- When the IUS tips are in the correct position (slightly protruding), pinch and hold the proximal end of the tube firmly to maintain rod position
- The proximal end of the insertion tube will be approximately at the top of the first indent on the rod



Loading the IUS Into the Inserter

Step 7: Check that the IUS is correctly loaded

- ✓ The IUS is completely within the insertion tube with the knobs of the arms forming a hemispherical dome at the top of the tube
- ✓ The top of the rod is touching the bottom of the IUS
- ✓ The blue threads are hanging through the end of the insertion tube
- ✓ The flange is marking the depth of the uterus based on pre-insertion sounding

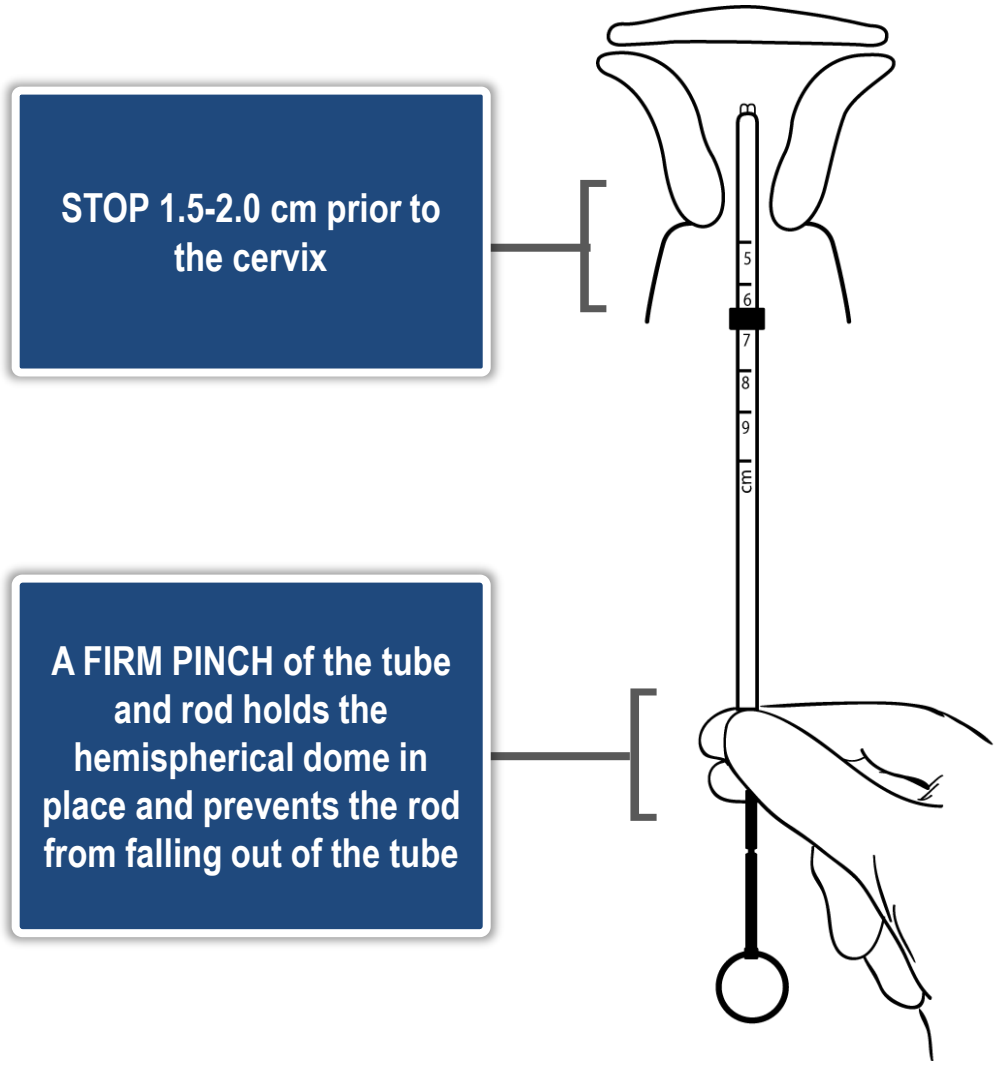
Loading the IUS Into the Inserter

Step 8: Remove insertion tube from the pouch

- Remove the loaded IUS insertion tube from the pouch while holding the lower end of the tube firmly between your fingers and thumb
- If not using sterile gloves, do not touch the flange and any part of the insertion tube above the flange during this step and through the IUS insertion procedure

IUS Insertion Into the Uterus

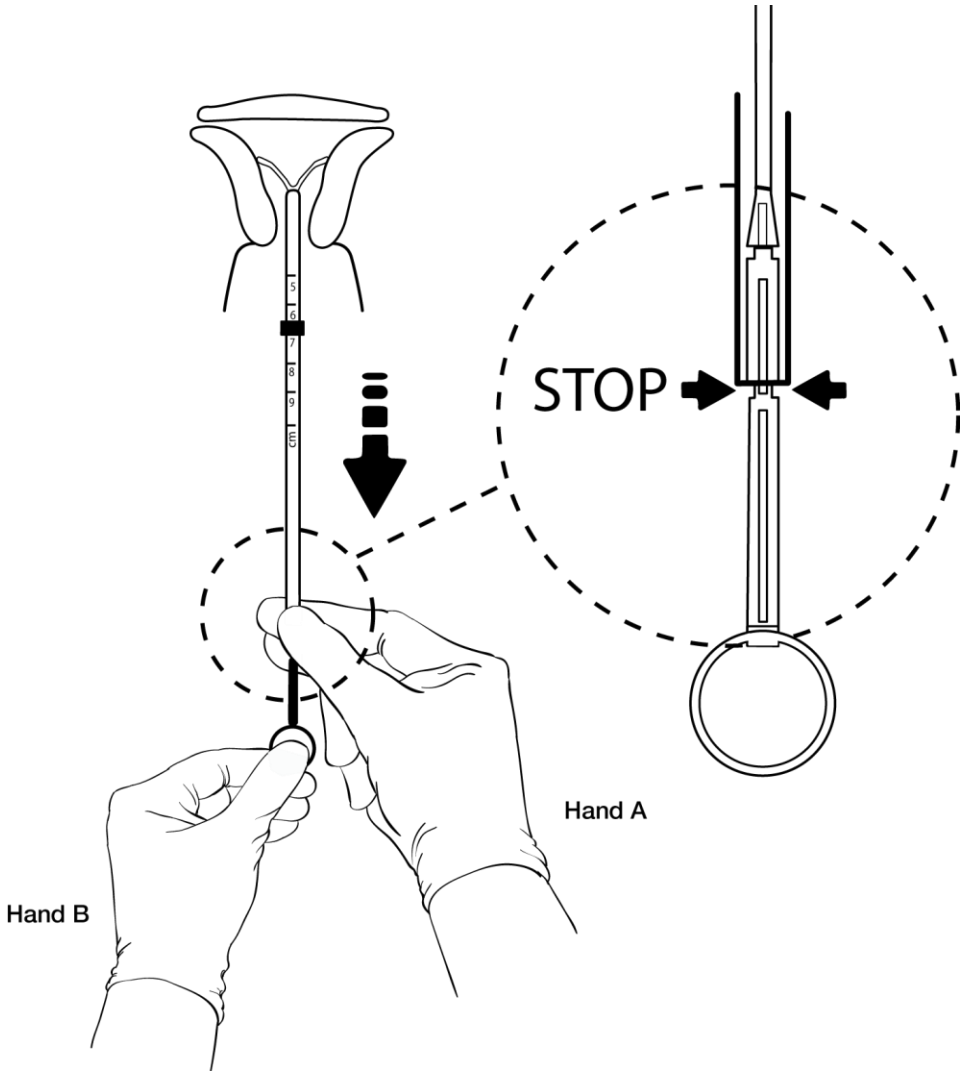
Step 1: Insert IUS into the uterus



- Apply gentle traction on the tenaculum to straighten the alignment of the cervical canal and uterine cavity
- While still firmly pinching the proximal end of the insertion tube, slide the loaded IUS insertion tube through the cervical canal until the upper edge of the flange is approximately 1.5–2.0 cm from the cervix
- DO NOT advance flange to the cervix at this step
- DO NOT force the inserter. If necessary, dilate the cervical canal

IUS Insertion Into the Uterus

Step 2 and 3: Deploy IUS

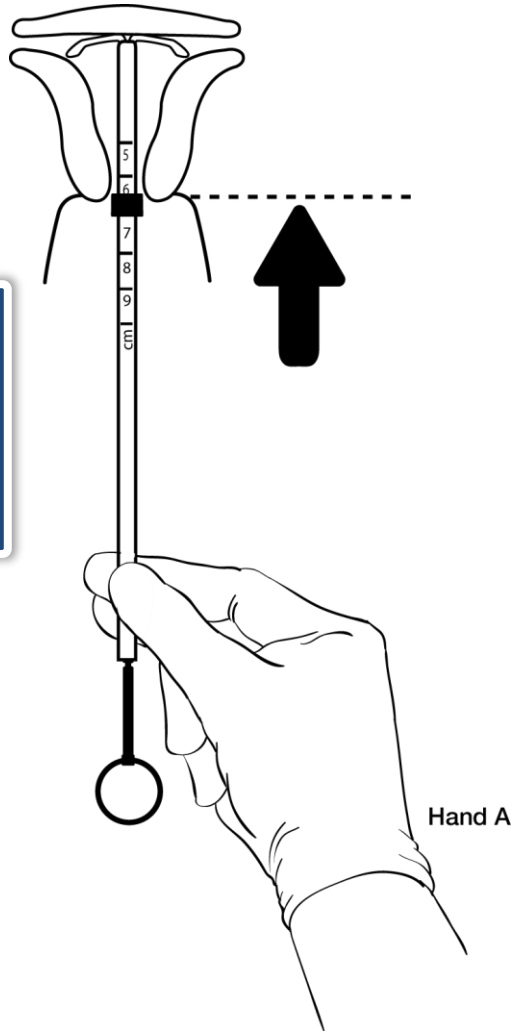


- Release hold on tenaculum
- Hold the insertion tube with the fingers of one hand (Hand A) and the rod with the fingers of other hand (Hand B)
- Hold the rod still with Hand B, relax the firmness of the pinch on the tube, and pull the insertion tube back with Hand A to the edge of the second indent of the rod
- Wait 10 – 15 seconds for the arms of the IUS to fully open

IUS Insertion Into the Uterus

Step 4: Advance IUS to fundus

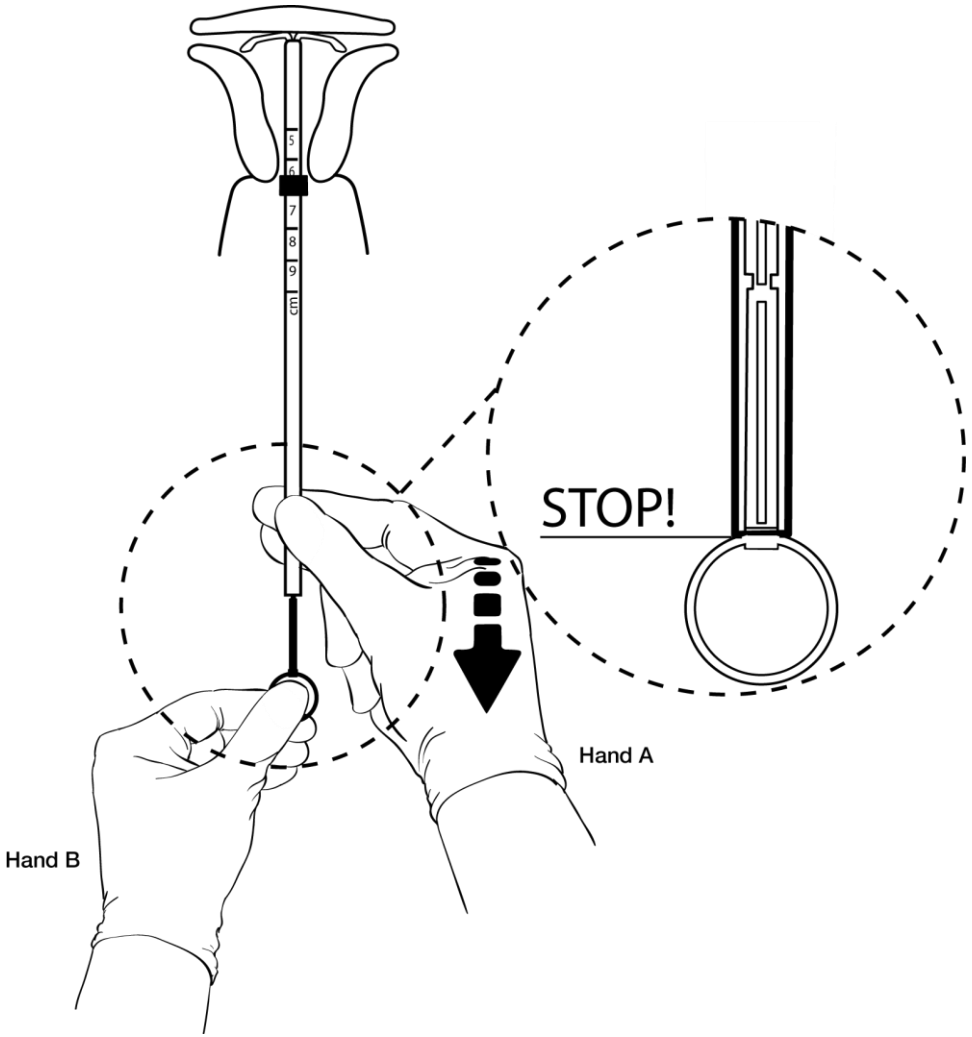
Fundal positioning is important to prevent expulsion



- Apply gentle traction with tenaculum before advancing the IUS
- With Hand A still holding the proximal end of the tube, advance both the insertion tube and rod simultaneously up to the uterine fundus
- You will feel slight resistance when the IUS is at the fundus
- The flange should be touching the cervix when the IUS reaches the uterine fundus

IUS Insertion Into the Uterus

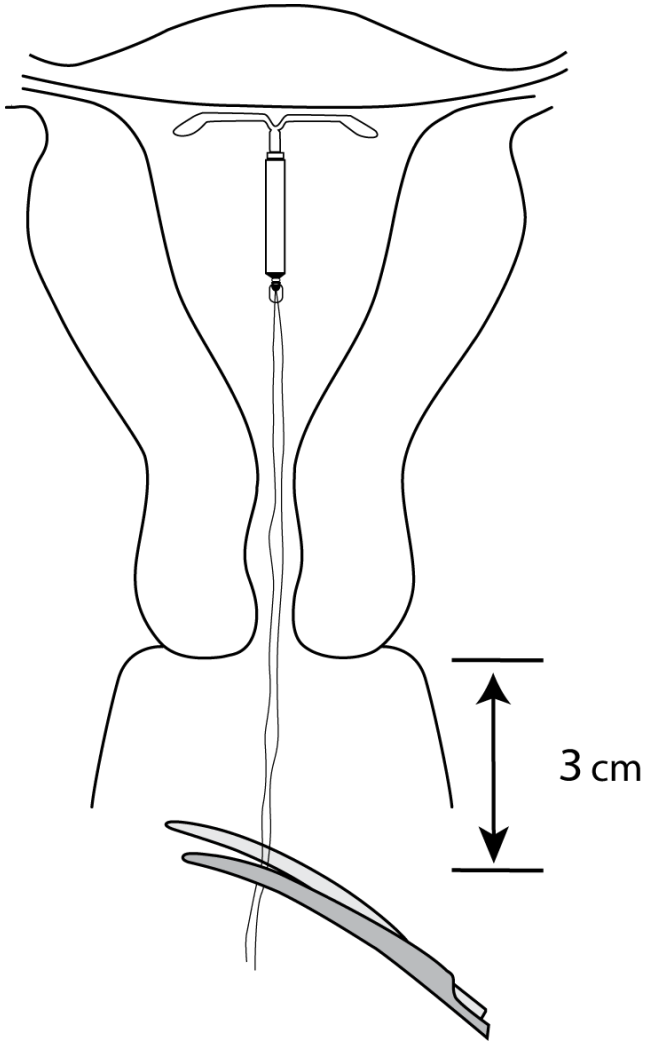
Steps 5-7: Release the IUS and withdraw the inserter



- Hold the rod still with Hand B while pulling the insertion tube back with Hand A to the ring of the rod
- While holding the inserter tube firmly in place with Hand A, withdraw the rod from the insertion tube all the way out to prevent the rod from catching on the knot at the lower end of the IUS
- Completely remove the insertion tube

IUS Insertion Into the Uterus

Step 8: Cut the threads



- Use blunt-tipped sharp scissors to cut the IUS threads perpendicular to the thread length leaving about 3 cm outside of the cervix
- *Cutting threads at an angle may leave sharp ends*
- Do not apply tension or pull on the threads when cutting to prevent displacing the IUS

Important Information to Consider During or After Insertion

If you suspect the IUS is not in the correct position:

- Check insertion with an ultrasound or other appropriate radiologic test
- If incorrect insertion is suspected, remove AVIBELA
  - A removed AVIBELA must not be re-inserted

If insertion is difficult because the uterus cannot be appropriately instrumented, the following measures can be considered:

- Use of cervical anesthesia to make sounding and manipulation more tolerable
- Use of dilators to dilate the cervix if needed to allow passage of the sound
- Abdominal ultrasound guidance during dilation and/or insertion
- If there is clinical concern, exceptional pain, or bleeding during or after insertion, take appropriate steps, such as physical examination and ultrasound, immediately to exclude perforation

Patient Counseling, Record-Keeping & Follow-Up

- Counsel the patient on what to expect following AVIBELA insertion
  - Review the signs and symptoms of expulsion
- Prescribe analgesics, if indicated
- Re-examine and evaluation patients 4 to 6 weeks after insertion and once a year thereafter, or more frequently if clinically indicated
  - You should check the strings during each routine and follow-up visit

REMOVAL OF AVIBELA

Timing of Removal of AVIBELA

- If pregnancy is desired, AVIBELA can be removed at any time
- If pregnancy is not desired, AVIBELA can be removed at any time; however, a contraception method should be started prior to removal of AVIBELA
  - Counsel your patient that if she is at risk of pregnancy if she has intercourse in the week prior to removal without use of a backup contraceptive method
- AVIBELA should be removed at the end of the approved duration of use
  - AVIBELA can be replaced at the time of removal with a new AVIBELA if continued contraceptive protection is desired

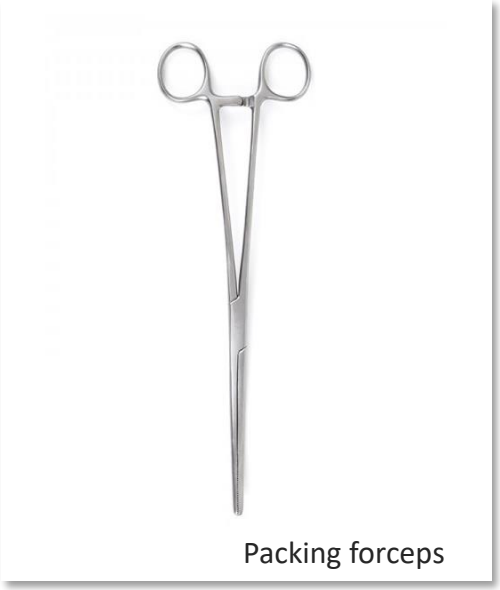
Items for Removal

Ensure all needed items for AVIBELA removal are readily available:

- Gloves
- Sterile speculum
- Sterile forceps

Additional items that may be required could include:

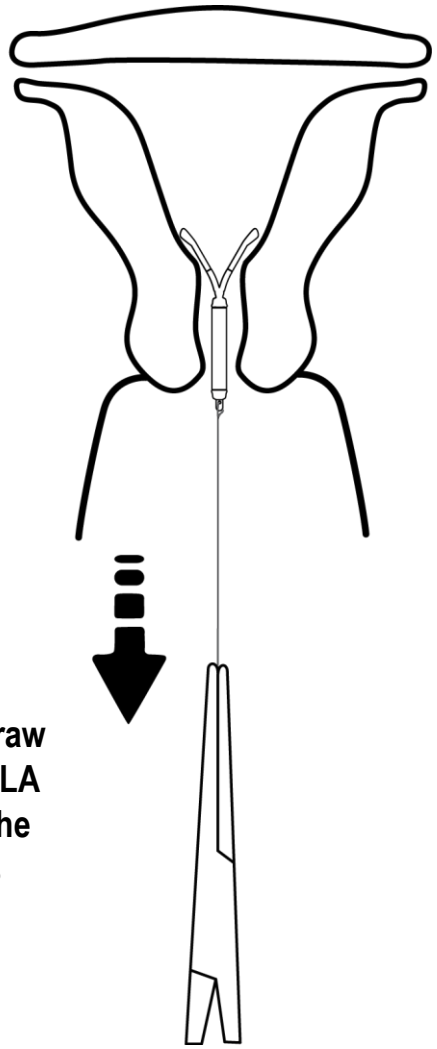
- Local anesthetic, needle, and syringe
- Sterile os finder, and/or cervical dilators
- Ultrasound with abdominal probe
- Sterile tenaculum
- Antiseptic solution
- Sterile, long, narrow forceps or intrauterine thread remover



Packing forceps

Alligator forceps

AVIBELA Removal Instructions



- With the patient comfortably in lithotomy position, place a speculum and visualize the cervix
- When the threads are visible, remove AVIBELA by applying gentle traction on the threads with forceps
  - If the IUS cannot be removed with traction on the threads, perform an ultrasound to confirm the location of the IUS
  - If the IUS is in the uterus, use long, narrow forceps to grasp AVIBELA
- Removal may be associated with some pain and/or bleeding or vasovagal reactions (e.g., syncope, bradycardia, or seizure), especially in patients with a predisposition to these conditions

AVIBELA Removal Instructions, continued

- If the threads of AVIBELA are not visible determine location of the IUS by ultrasound examination
  - If the IUS is in the uterine cavity, thoroughly cleanse the cervix and vagina with antiseptic solution
  - Use a thread retriever to capture the threads or a long, narrow forceps (e.g., Alligator forceps) to grasp AVIBELA
- Consider use of a tenaculum, cervical anesthesia, cervical dilators, and/or ultrasound guidance as needed
- If AVIBELA cannot be removed using the above techniques, consider hysteroscopic evaluation for removal
- If the IUS is not in the uterine cavity, consider an abdominal x-ray or CT scan to evaluate if the IUS is in the abdominal cavity
  - Consider laparoscopic evaluation for removal, as clinically indicated
- After removal, examine the system to ensure it is intact

Continuation of Contraception After Removal

- Women who wish to continue using AVIBELA or another intrauterine contraceptive:
  - Insertion can occur immediately after removal
- Women with regular cycles who want to start a different birth control method:
  - Either remove AVIBELA during the first 7 days of the menstrual cycle and start the new method, OR start the new method at least 7 days prior to AVIBELA removal
- Women with irregular cycles or amenorrhea who want to start a different birth control method:
  - Start the new method at least 7 days before AVIBELA removal

Continuation of Contraception After Removal

- If AVIBELA is removed but no other contraceptive method has already been started, the new method can be started on the day AVIBELA is removed
- To prevent pregnancy, the patient should:
  - Use a backup barrier method of contraception (e.g., condoms and spermicide), OR
  - Abstain from vaginal intercourse for 7 days

SELECTED IMPORTANT SAFETY INFORMATION

Contraindications to Use of AVIBELA

- Pregnancy
- For use as post-coital contraception (emergency contraception)
- Acute pelvic inflammatory disease (PID) or endometritis or a history of PID unless there has been a subsequent intrauterine pregnancy
- Infected abortion in the past 3 months
- Known or suspected uterine or cervical neoplasia
- Acute liver disease or liver tumor (benign or malignant)
- Conditions associated with increased susceptibility to pelvic infections
- Congenital or acquired uterine anomaly, including fibroids, that distorts the uterine cavity and would be incompatible with correct IUS placement
- Uterine bleeding of unknown etiology
- Untreated acute cervicitis or vaginitis, including bacterial vaginosis, known chlamydial or gonococcal cervical infection, or other lower genital tract infections until infection is controlled
- Known or suspected breast cancer or other hormone-sensitive cancer, now or in the past
- A previously inserted IUS that has not been removed
- A history of hypersensitivity reaction to any component of AVIBELA. Reactions may include rash, urticaria, and angioedema

Special Warnings & Precautions for Use

Medical examination

- Obtain a complete medical and social history, including partner status, to determine conditions that might influence the selection of an IUS for contraception and/or heavy menstrual bleeding
- Exclude underlying endometrial pathology (e.g., polyps or cancer) prior to the insertion of AVIBELA in women with persistent or uncharacteristic bleeding because irregular bleeding/spotting is common during the first months of AVIBELA use and may preclude adequate assessment after insertion. AVIBELA is contraindicated in women with uterine bleeding of unknown etiology
- Exclude underlying congenital or acquired uterine anomalies, including fibroids, that distort the uterine cavity and would be incompatible with correct IUS placement
- Ensure a previously inserted IUS has been removed prior to insertion of AVIBELA
- Assess whether the woman is at increased risk of infection (e.g., leukemia, acquired immune deficiency syndrome [AIDS], IV drug abuse), or has a history of PID unless there has been a subsequent intrauterine pregnancy. AVIBELA does not protect against HIV/STI transmission

Special Warnings & Precautions for Use

Conditions under which AVIBELA can be used by caution

- Use AVIBELA with caution after careful assessment if any of the following conditions exist, and consider removal of the IUS if any of them arise during use:
  - Coagulopathy or use of anticoagulants
  - Migraine, focal migraine with asymmetrical visual loss, or other symptoms indicating transient cerebral ischemia
  - Exceptionally severe or frequent headache
  - Marked increase of blood pressure
  - Severe arterial disease such as stroke or myocardial infarction

- Consider removing AVIBELA if any of the following conditions arise during use:
  - Uterine or cervical malignancy
  - Jaundice

Pregnancy related risks with AVIBELA

- In case of an accidental pregnancy with AVIBELA in situ, advise a woman of the increased risks for pregnancy complications, including miscarriage, premature labor, premature delivery, infection and sepsis. Ectopic pregnancy should be excluded, and removal of the system should be considered

- Removal of AVIBELA or probing of the uterus may result in spontaneous abortion. Should these procedures not be possible or if the woman wishes to continue the pregnancy, the woman should be informed about these risks, and accordingly, such pregnancies should be closely monitored. Prenatal care should include counseling about these risks and that she should report immediately any flu-like symptoms, fever, chills, cramping, pain, bleeding, vaginal discharge or leakage of fluid, or any other symptom that suggests complications of the pregnancy

Adverse reactions to AVIBELA

- Undesirable effects are more common during the first months after the insertion and generally subside during prolonged use
- In a large clinical trial of 1751 women using AVIBELA for contraception, very common undesirable effects (occurring in more than 10% of users) include vaginal bacterial infections, vulvovaginal mycotic infections, nausea or vomiting, and acne
- Cases of sepsis (including group A streptococcal sepsis) have been reported following insertions with hormonal IUSs
- The following adverse reactions have been reported in connection with the insertion or removal procedure of AVIBELA: pain, bleeding, and insertion-related vasovagal reaction with dizziness or syncope. The procedure may also precipitate a seizure in patients with epilepsy
- The removal threads may be felt by the partner during intercourse
- Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product
  - Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system or to the supplier

AVIBELA Manufacturing & Supplier Information

AVIBELA is manufactured by:

Odyssea Pharma sprl,
an affiliated company of AbbVie Inc.
Rue du Travail, 16
B-4460
Grâce-Hollogne, Belgium
for:

Impact RH360 LLC
San Francisco, CA
USA