Sophie is a hypothetical patient. Individual results may vary.

Childhood. Uninterrupted.

Uninterrupted luteinizing hormone suppression through Month 12 after the first month of therapy

SUPPRELIN® Long-Acting: Surgical Overview

Once-yearly SUPPRELIN® Long-Acting (histrelin acetate) implant is the longest-acting **CPP therapy** available and one dose is FDA-approved to treat CPP for 12 months[1*]

***Be sure to explain to the parents or caregivers of the patient that the child will need regular exams and blood tests to check for signs of puberty. Implant must be removed and may be replaced every 12 months at the physician's discretion until appropriate time point for the onset of puberty.**

INDICATION

- SUPPRELIN® LA (histrelin acetate) subcutaneous implant is indicated for the treatment of children with central precocious puberty (CPP).
- Children with CPP (neurogenic or idiopathic) have an early onset of secondary sexual characteristics (earlier than 8 years of age in females and 9 years of age in males). They also show a significantly advanced bone age that can result in diminished adult height attainment.
- Prior to initiation of treatment, a clinical diagnosis of CPP should be confirmed by measurement of blood concentrations of total sex steroids, luteinizing hormone (LH) and follicle stimulating hormone (FSH) following stimulation with a GnRH analog, and assessment of bone age versus chronological age. Baseline evaluations should include height and weight measurements, diagnostic imaging of the brain (to rule out intracranial tumor), pelvic/testicular/adrenal ultrasound (to rule out steroid secreting tumors), human chorionic gonadotropin levels (to rule out a chorionic gonadotropin secreting tumor), and adrenal steroids to exclude congenital adrenal hyperplasia.

IMPORTANT SAFETY INFORMATION ABOUT SUPPRELIN® LA

- SUPPRELIN® LA is contraindicated in patients who are hypersensitive to gonadotropin releasing hormone (GnRH) or GnRH agonist analogs and in females who are or may become pregnant while receiving the drug. SUPPRELIN® LA may cause fetal harm or spontaneous abortion when administered to pregnant patients. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

Please see additional Important Safety Information about SUPPRELIN® LA on last page.

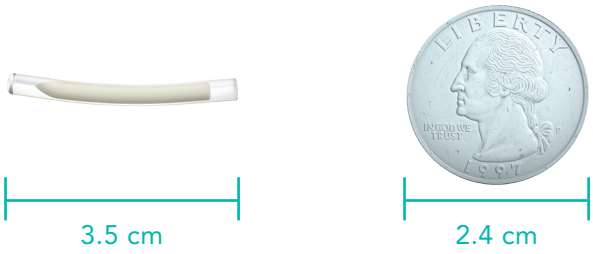
Please click here for full Prescribing Information.

ONCE-YEARLY *Uninterrupted*
SUPPRELIN® LA
(histrelin acetate) subcutaneous implant

SUPPRELIN® Long-Acting—Treat once yearly[1]

SUPPRELIN® Long-Acting is a soft, flexible implant designed to deliver **medication for one full year.**[1]

The Implant Is a Small, Thin, Flexible Tube Measuring 3.5 cm by 3 mm[1]



Not to scale.

The SUPPRELIN® LA implant is packaged hydrated in a 3.5-mL glass vial containing 2 mL of sterile 1.8% sodium chloride solution, so that it is primed for immediate release of the drug upon insertion. The implant should be kept refrigerated (2-8°C) in its sealed vial, pouch, and carton, until needed for the procedure. Once removed from refrigeration, the vial containing the implant (still in its unopened pouch and carton) may remain at room temperature for up to 7 days, if necessary, before being used. If not used in that time, the packaged implant may again be properly refrigerated until the expiration date on the carton.[1]

- The recommended dose is one 50-mg implant, surgically inserted subcutaneously into the inner aspect of the arm once every 12 months[1]
- Delivers approximately 65 mcg histrelin acetate per day over 12 months[1]
- SUPPRELIN® LA should be removed after 12 months of therapy (the implant has been designed to allow for a few additional weeks of histrelin acetate release, in order to allow flexibility of medical appointments)[1]
- At the time an implant is removed, another implant may be inserted to continue therapy. Discontinuation of SUPPRELIN® LA should be considered at the discretion of the physician and at the appropriate time point for the onset of puberty (approximately 11 years for females and 12 years for males)[1]
- One month after removal, histrelin levels were undetectable and LH returned to pubertal levels (n=4)—demonstrating that the suppression obtained with SUPPRELIN® LA was completely reversible in a clinical trial[2]

IMPORTANT SAFETY INFORMATION ABOUT SUPPRELIN® LA (cont)

- SUPPRELIN® LA, like other GnRH agonists, initially causes a transient increase in serum concentrations of estradiol in females and testosterone in both sexes during the first week of treatment, with worsening of symptoms or onset of new symptoms during this period. Within 4 weeks of therapy, gonadal steroid suppression occurs and manifestations of puberty decrease.

Please see additional Important Safety Information about SUPPRELIN® LA on last page.

Please click here for full Prescribing Information.

ONCE-YEARLY *Uninterrupted*
SUPPRELIN® LA
(histrelin acetate) subcutaneous implant

The SUPPRELIN® LA Implantation Kit[1]

SUPPRELIN® LA is supplied in a corrugated shipping carton that contains 2 inner cartons: a small one for the vial containing the SUPPRELIN® LA implant, which is shipped with a cold pack inside a polystyrene cooler that must be refrigerated upon arrival, and a larger one comprising the Implantation Kit, which must not be refrigerated, for use during insertion or removal of SUPPRELIN® LA.[1] The SUPPRELIN® LA Implantation Kit includes all the necessary components for the insertion and removal of the implant (sterile gloves not included).

The Implantation Kit is to be stored at room temperature and should ***NOT*** be refrigerated.

Components:

- 1 #15 disposable scalpel
- 1 syringe with 18-gauge needle
- 1 25-gauge 1.5" needle
- 1 SS mosquito clamp
- 4 packages gauze sponges
- 2 packages alcohol swabs
- 1 fenestrated drape
- 1 non-fenestrated drape
- 1 package skin antiseptic swab
- 1 package surgical closure strips
- 1 package coated absorbable suture
- 1 package cohesive bandage
- 1 vial local anesthetic (manufacturer may vary)
- 1 implant insertion tool
- 1 benzoin tincture antiseptic
- Prescribing Information, including Medication Guide*

*Item not shown

IMPORTANT SAFETY INFORMATION ABOUT SUPPRELIN® LA (cont)

- Implant insertion and removal is a surgical procedure and should utilize aseptic technique. Careful adherence to the recommended insertion and removal procedures is recommended to avoid potential complications. Proper surgical technique is critical in minimizing adverse events related to the insertion and the removal of the histrelin implant. On occasion, localizing and/or removal of implant products have been difficult and imaging techniques were used including ultrasound, CT, or MRI (this implant is not radiopaque). In some cases, the implant broke during removal and multiple pieces were recovered. Rare events of spontaneous extrusion have been observed in clinical trials. During SUPPRELIN® LA treatment, patients should be evaluated for evidence of clinical and biochemical suppression of CPP manifestation.

Please see additional Important Safety Information about SUPPRELIN® LA on last page.

Please click here for full Prescribing Information.

ONCE-YEARLY *Uninterrupted*
SUPPRELIN® LA
(histrelin acetate) subcutaneous implant

Suggested insertion procedure[1]

Insertion of the SUPPRELIN® LA implant is a minimally invasive surgical procedure. Sterile gloves and aseptic technique must be used to minimize any chance of infection.[1]

This recommended procedure is intended to provide guidance for the insertion and removal of SUPPRELIN® LA. The actual procedure used, however, is at the discretion of the qualified healthcare provider. For more details, please consult the full Prescribing Information.

SETTING UP THE STERILE FIELD

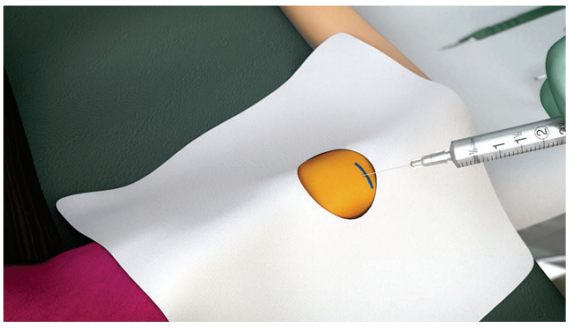
NOTE THAT THE KIT BOX AND ALL PACKAGING ARE NOT STERILE and should be kept off the Sterile Field drape. **DO NOT PLACE THE VIAL OF LOCAL ANESTHETIC OR THE VIAL CONTAINING THE IMPLANT ONTO THE DRAPE,** as the exterior surface of these vials is not sterile.[1]

1

PREPARE PATIENT[1]

- Select nondominant arm if possible
- Implant site should be approximately halfway between the shoulder and the elbow and in line with the crease between the biceps and triceps
- Prep incision site: Swab with topical antiseptic
- Prep implant site: Overlay site with fenestrated Sterile Field drape (provided) so that the opening is over the insertion site

The patient should be on his/her back, with the arm containing the implant positioned, either bent or extended, so that the physician has ready access to the inner aspect of the upper arm.



2

ADMINISTER ANESTHETIC[1]

- The method of anesthesia utilized (i.e., local, conscious sedation, general) is at the discretion of the healthcare provider
- If using local anesthetic, and after determining the absence of known allergies to the anesthetic agent, inject anesthetic into the subcutaneous tissue at the planned insertion site and infiltrate a little more than one inch along the length of the site

IMPORTANT SAFETY INFORMATION ABOUT SUPPRELIN® LA (cont)

- Psychiatric events have been reported in patients taking GnRH agonists, including SUPPRELIN® LA. Postmarketing reports with this class of drugs include symptoms of emotional lability, such as crying, irritability, impatience, anger, and aggression. Depression, including rare reports of suicidal ideation and attempt, has been reported for GnRH agonists, including SUPPRELIN® LA, in children treated for central precocious puberty. Many, but not all, of these patients had a history of psychiatric illness or other comorbidities with an increased risk of depression. Monitor for development or worsening of psychiatric symptoms during treatment with SUPPRELIN® LA.

3

PREPARE IMPLANT[1]

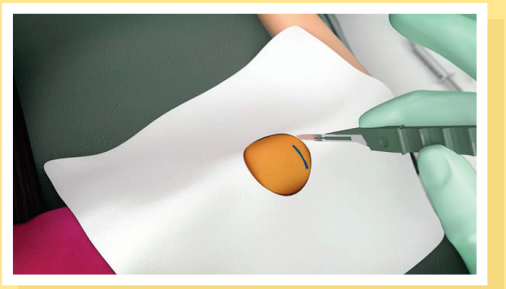
- Push the green retraction button forward; the button of the Insertion Tool should be locked in place with the cannula fully extended
- Open the vial by removing the metal band and stopper and carefully pour the sterile contents (implant and sterile saline) onto the Sterile Field drape. The implant can then be handled with sterile gloves or with the sterile mosquito clamp provided
- If implant is slightly curved, gently roll between thumb and forefinger to make the implant more symmetrical
- **Avoid bending or pinching the implant**
- When inserting the implant into the cannula, **DO NOT FORCE** the implant. If resistance is felt, the implant should be removed and manually manipulated or rolled, as needed, and re-inserted into the cannula. When fully inserted, only the tip of the implant should be visible at the beveled end of the cannula

IMPORTANT SAFETY INFORMATION ABOUT SUPPRELIN® LA (cont)

- Postmarketing reports of convulsions have been observed in patients receiving GnRH agonists, including SUPPRELIN® LA. Reports with GnRH agonists have included patients with a history of seizures, epilepsy, cerebrovascular disorders, central nervous system anomalies or tumors, and patients on concomitant medications that have been associated with convulsions such as bupropion and SSRIs. Convulsions have also been reported in patients in the absence of any of the conditions mentioned above.

4 MAKE THE INCISION & INSERT IMPLANT[1]

- Make an incision transverse to the long axis of the arm, long enough to allow insertion of the cannula
- For easier insertion, create a subcutaneous pocket along the line of the incision, using the cannula of the loaded insertion tool or other appropriate surgical tool
- Carefully insert the tip of the cannula into the incision and advance into the subcutaneous pocket up to the inscribed black line on the cannula, but no farther. Be sure to visibly raise the skin (known as tenting) at all times during the pocket-making and insertion procedures to ensure correct subcutaneous placement (just under the skin) of the implant. The insertion tool **SHOULD NOT ENTER MUSCLE TISSUE**
- **DO NOT DEPRESS THE GREEN RETRACTION BUTTON ON THE TOOL WHILE INSERTING OR ADVANCING THE TOOL INTO THE INCISION.** Pull the tool back, almost to the beveled tip of the cannula, and advance the tool forward again, so that the cannula re-enters the pocket completely, but no farther than the inscribed black line. Be sure to keep the insertion path just immediately subcutaneous
- Hold the insertion tool in place and depress the green retraction button to release the locking mechanism
- Slide the green retraction button back toward the handle while holding the insertion tool in place. **DO NOT FURTHER ADVANCE THE CANNULA ONCE THE RETRACTION PROCESS HAS STARTED**
- Retraction withdraws the cannula, leaving the implant in the subcutaneous tissue. Do not withdraw the insertion tool until the button is fully retracted or the implant may be pulled partially out of the incision. Once the retraction is complete, the tool can be fully withdrawn
- Confirm proper placement of the implant by palpating the surface of the arm
- After implantation, briefly cover the site with a sterile gauze pad and apply pressure to ensure hemostasis



It may be helpful during the process of retraction and withdrawal of the cannula to apply pressure to the skin over the implant, to help ensure that the implant remains in the subcutaneous pocket.

5 CLOSE INCISION[1]

- Close with surgical strips or absorbable sutures. Knots should face inside the incision
- To improve adhesion of the strips, you can apply benzoin tincture antiseptic (provided) to the skin, and let it dry, before applying the adhesive strips
- Cover the incision with sterile gauze pads
- Secure the gauze pads with bandage provided

Please provide the patient's parent or guardian with a Medication Guide, which includes information about the implant and instructions on proper care of the insertion site.

IMPORTANT SAFETY INFORMATION ABOUT SUPPRELIN® LA (cont)

- LH, FSH and estradiol or testosterone should be monitored at 1 month post implantation, then every 6 months. Every 6-12 months, height and bone age should be assessed.

Please see additional Important Safety Information about SUPPRELIN® LA on last page.

Please click here for full Prescribing Information.

ONCE-YEARLY *Uninterrupted*
SUPPRELIN® LA
(histrelin acetate) subcutaneous implant

Suggested removal procedure[1]

Removal of the SUPPRELIN® LA implant is a surgical procedure. Sterile gloves and aseptic technique must be used to minimize any chance of infection.

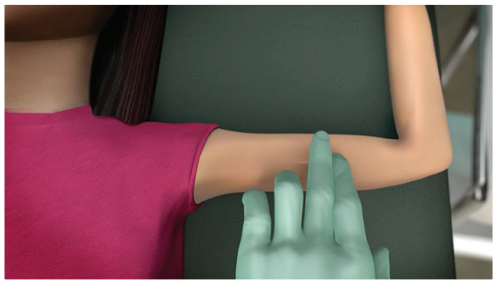
SETTING UP THE STERILE FIELD

NOTE THAT THE KIT BOX AND ALL PACKAGING ARE NOT STERILE and should be kept off the Sterile Field drape. **DO NOT PLACE THE VIAL OF LOCAL ANESTHETIC OR THE VIAL CONTAINING THE IMPLANT ONTO THE DRAPE,** as the exterior surface of these vials is not sterile.[1]

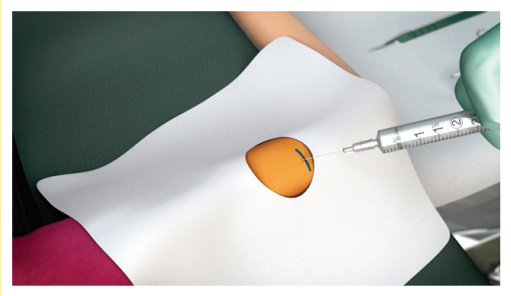
1

PREP INCISION SITE[1]

- Palpate skin around previous incision to locate the implant
- Use ultrasound, CT, or MRI if the implant is difficult to locate, or is not palpable **(the implant is not radiopaque)**
- Swab with topical antiseptic
- Overlay site with fenestrated Sterile Field drape so that the opening is over the previous insertion site



The patient should be on his/her back, with the arm containing the implant positioned, either bent or extended, so that the physician has ready access to the inner aspect of the upper arm.



2

ADMINISTER ANESTHETIC[1]

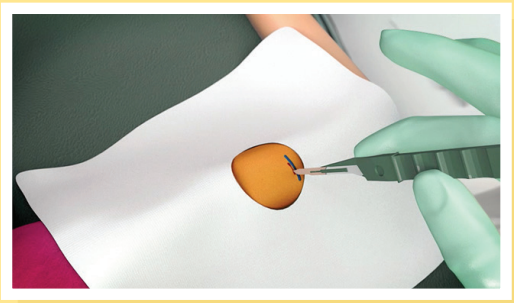
- The method of anesthesia utilized (i.e., local, conscious sedation, general) is at the discretion of the healthcare provider
- If using local anesthesia, and after determining the absence of known allergies to the anesthetic agent, inject the anesthetic subcutaneously at and around the site of the previous implant

IMPORTANT SAFETY INFORMATION ABOUT SUPPRELIN® LA (cont)

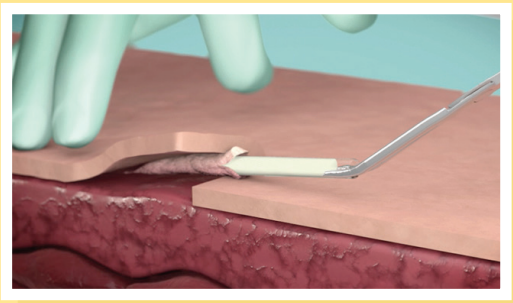
- In clinical trials, the most common adverse reactions involved the implant site and included discomfort, bruising, soreness, pain, tingling, itching, erythema, and implant area protrusion and swelling.
- The safety and effectiveness in pediatric patients under the age of 2 years have not been established. The use of SUPPRELIN® LA in children under 2 years is not recommended.

3

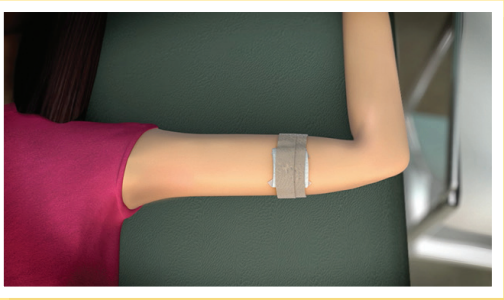
REMOVE IMPLANT[1]



- Make an incision wide enough to allow the implant to be easily removed, or large enough for the bore of the cannula of the Insertion Tool provided, if a new implant is inserted. In order to facilitate the removal of the implant, it may be necessary to palpate the head of the implant through the incision using your smallest finger, especially if the head of the implant is not readily visible. In addition, you may need to push down on the distal end of the implant and "massage it forward" towards the incision
- A pseudocapsule of tissue may have formed over and around the implant
- Carefully nick the tip of the pseudocapsule to reveal the tip of the implant
- Gently but securely grasp the tip of the implant with the provided sterile mosquito clamp
- Remove the implant from the incision; dispose of in a proper manner, treating it like any other bio-waste; briefly cover the site with a sterile gauze pad, applying pressure to ensure hemostasis; if inserting a new implant, follow the suggested procedures for insertion
- You may insert the new implant into the same "pocket" as the removed implant, or make a new incision at a different site in the same arm or in the contralateral arm
- If a new implant is not to be inserted, proceed to close the incision



In some cases the implant broke during removal and multiple pieces were recovered. Confirm that the entire implant has been removed. If the implant was not retrieved completely, the remaining pieces should be removed following the instructions in the Suggested Removal Procedure section.



4

CLOSE INCISION[1]

- Close with surgical strips or absorbable sutures. Knots should face inside the incision
- To improve adhesion of the strips, you can apply benzoin tincture antiseptic (provided) to the skin, and let it dry, before applying the adhesive strips
- Cover the incision with sterile gauze pads
- Secure the gauze pads with bandage provided

Please provide the patient's parent or guardian with a Medication Guide, which includes information about the implant and instructions on proper care of the insertion site.

IMPORTANT SAFETY INFORMATION ABOUT SUPPRELIN® LA (cont)

- SUPPRELIN® LA is contraindicated in patients who are hypersensitive to gonadotropin releasing hormone (GnRH) or GnRH agonist analogs and in females who are or may become pregnant while receiving the drug. SUPPRELIN® LA may cause fetal harm or spontaneous abortion when administered to pregnant patients. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

Billing and coding

NDC#: 67979-002-01	**STRENGTH:** 50 mg (histrelin acetate)
PACKAGE SIZE: One (1) Subcutaneous Implant and Insertion Kit	

HCPCS LEVEL 1 (CPT CODES) FOR PHYSICIAN'S PROFESSIONAL CHARGES
11981 Insertion, non-biodegradable drug delivery implant
11982 Removal, non-biodegradable drug delivery implant
11983 Removal with reinsertion, non-biodegradable drug delivery implant

HCPCS LEVEL 2 CODE	**J9226** Histrelin implant (SUPPRELIN® LA), 50 mg
ICD-10 CM DIAGNOSIS CODE	**E22.8** Other hyperfunction of pituitary gland
AMBULATORY PAYMENT CLASSIFICATION PROCEDURE CODE	**1142** SUPPRELIN® LA implant
PHYSICIAN OFFICE BILLING CODES	**99211-99215** Office or other outpatient visit **99354 or 99355** Prolonged service, office

EVALUATION AND MANAGEMENT (OFFICE OR OTHER OUTPATIENT VISIT)	
99201 Office outpt new 10 min	**99211** Office outpt est 5 min
99202 Office outpt new 20 min	**99212** Office outpt est 10 min
99203 Office outpt new 30 min	**99213** Office outpt est 15 min
99204 Office outpt new 45 min	**99214** Office outpt est 25 min
99205 Office outpt new 60 min	**99215** Office outpt est 40 min

REVENUE CODES (HOSPITAL OUTPATIENT BILLING)	
0250 General pharmacy	**0761** Treatment room
0636 Drugs requiring detailed coding	**0360** Operating room
0510 Outpatient clinic visit	

Coding is part of the clinical decision. Please use codes that most accurately reflect the procedures performed. Suggestions by Endo Pharmaceuticals Inc. do not guarantee reimbursement or take the place of professional coding advice.

IMPORTANT SAFETY INFORMATION ABOUT SUPPRELIN® LA (cont)

- SUPPRELIN® LA, like other GnRH agonists, initially causes a transient increase in serum concentrations of estradiol in females and testosterone in both sexes during the first week of treatment, with worsening of symptoms or onset of new symptoms during this period. Within 4 weeks of therapy, gonadal steroid suppression occurs and manifestations of puberty decrease.

Please see additional Important Safety Information about SUPPRELIN® LA on last page.

Please click here for full Prescribing Information.

ONCE-YEARLY *Uninterrupted*
SUPPRELIN® LA
(histrelin acetate) subcutaneous implant

LEARN MORE at www.supprelinla.com

Reimbursement questions? Call The SUPPRELIN® LA Support Center at 1-855-270-0123

Program specialists are available toll-free, Monday through Friday, 8 AM to 8 PM ET.

INDICATION

- SUPPRELIN® LA (histrelin acetate) subcutaneous implant is indicated for the treatment of children with central precocious puberty (CPP).
- Children with CPP (neurogenic or idiopathic) have an early onset of secondary sexual characteristics (earlier than 8 years of age in females and 9 years of age in males). They also show a significantly advanced bone age that can result in diminished adult height attainment.
- Prior to initiation of treatment, a clinical diagnosis of CPP should be confirmed by measurement of blood concentrations of total sex steroids, luteinizing hormone (LH) and follicle stimulating hormone (FSH) following stimulation with a GnRH analog, and assessment of bone age versus chronological age. Baseline evaluations should include height and weight measurements, diagnostic imaging of the brain (to rule out intracranial tumor), pelvic/testicular/adrenal ultrasound (to rule out steroid secreting tumors), human chorionic gonadotropin levels (to rule out a chorionic gonadotropin secreting tumor), and adrenal steroids to exclude congenital adrenal hyperplasia.

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- SUPPRELIN® LA, like other GnRH agonists, initially causes a transient increase in serum concentrations of estradiol in females and testosterone in both sexes during the first week of treatment, with worsening of symptoms or onset of new symptoms during this period. Within 4 weeks of therapy, gonadal steroid suppression occurs and manifestations of puberty decrease.
- Implant insertion and removal is a surgical procedure and should utilize aseptic technique. Careful adherence to the recommended insertion and removal procedures is recommended to avoid potential complications. Proper surgical technique is critical in minimizing adverse events related to the insertion and the removal of the histrelin implant. On occasion, localizing and/or removal of implant products have been difficult and imaging techniques were used including ultrasound, CT, or MRI (this implant is not radiopaque). In some cases, the implant broke during removal and multiple pieces were recovered. Rare events of spontaneous extrusion have been observed in clinical trials. During SUPPRELIN® LA treatment, patients should be evaluated for evidence of clinical and biochemical suppression of CPP manifestation.
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- Postmarketing reports of convulsions have been observed in patients receiving GnRH agonists, including SUPPRELIN® LA. Reports with GnRH agonists have included patients with a history of seizures, epilepsy, cerebrovascular disorders, central nervous system anomalies or tumors, and patients on concomitant medications that have been associated with convulsions such as bupropion and SSRIs. Convulsions have also been reported in patients in the absence of any of the conditions mentioned above.
- LH, FSH and estradiol or testosterone should be monitored at 1 month post implantation, then every 6 months. Every 6-12 months, height and bone age should be assessed.
- In clinical trials, the most common adverse reactions involved the implant site and included discomfort, bruising, soreness, pain, tingling, itching, erythema, and implant area protrusion and swelling.
- The safety and effectiveness in pediatric patients under the age of 2 years have not been established. The use of SUPPRELIN® LA in children under 2 years is not recommended.

References: 1. SUPPRELIN® LA [package insert]. Malvern, PA: Endo Pharmaceuticals Inc. **2.** Eugster EA, Clarke W, Kletter GB, et al. Efficacy and safety of histrelin subdermal implant in children with central precocious puberty: a multicenter trial. *J Clin Endocrinol Metab*. 2007;92(5):1697-1704.

Please click here for full Prescribing Information.

ONCE-YEARLY *Uninterrupted*
SUPPRELIN® LA
(histrelin acetate) subcutaneous implant

endo pharmaceuticals
an endo international company

Rx Only

SP-05439/March 2020 www.supprelinla.com 1-800-462-ENDO (3636)