

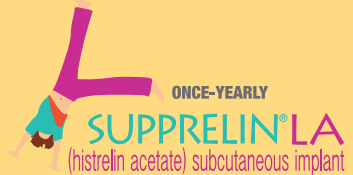
# Understanding Central Precocious Puberty

And the once-yearly  
treatment that lasts  
a full year

A guide for parents



Please see accompanying full Prescribing Information.





Demonstration unit only (contains no active ingredient)  
**3.5 cm x 3 mm hydrogel implant**

# You want the best for your child—today and in the future

That includes getting the useful information you can find on **central precocious puberty**. This booklet can help. It offers answers to common questions, information to address concerns, and input on treatment choices. Of course, because each child matures differently, your pediatrician and pediatric endocrinologist are always the best people to advise you about your child's health. But this booklet is a good place to begin understanding central precocious puberty and available treatment options.



Please see accompanying full Prescribing Information.

## Let's start by talking about puberty

Puberty can be summed up with one word: change. Whether puberty occurs when expected—between ages 8-13 in girls and ages 9-14 in boys<sup>1</sup>—or earlier, the changes are profound. These changes include sexual maturation, physical growth, and emotional shifts.

### How does puberty start?

The changes begin in the brain. The hypothalamus, a part of the brain, sends a signal to the pituitary gland. This signal—called a gonadotropin releasing hormone, or GnRH, for short—tells the pituitary to release larger amounts of hormones called gonadotropins. Gonadotropins go straight to the ovaries or to the testicles, where they tell the body to produce the sex hormones estrogen (for girls) or testosterone (for boys). This marks the start of puberty.



**Reference: 1.** Antoniazzi F, Zamboni G. Central precocious puberty: current treatment options. *Pediatr Drugs*. 2004;6(4):212-231.

The first noticeable signs of puberty occur as a result of these hormonal changes:

- For girls, these are breast “buds,” followed by pubic hair growth. Menstruation (periods) typically starts around age 12
- For boys, it is testicular enlargement and then pubic hair growth

Other signs of puberty can occur over the course of several years, and include:

- Appearance of underarm hair
- Adult body odor
- Facial hair and voice change in boys

## What about the “growth spurt”?

When puberty begins, an additional change takes place: children grow more rapidly. This is because sex steroids also have an impact on growth hormones. As a result, a child can grow several inches in a year. In girls, this growth spurt usually occurs at about the same time as other signs of puberty. In boys, the growth spurt occurs a little later, when testosterone levels are rising quickly.

## Do girls enter puberty earlier than boys?

It's true that girls usually enter puberty before boys, but only about 6 to 12 months earlier. Girls may seem to enter puberty long before boys because their first signs of puberty are more obvious. Breast development is easier to see than early signs of puberty in boys. And girls go through their growth spurts at the beginning of puberty, while boys go through the growth spurt towards the middle of puberty.

## What about moodiness—is that a sign of puberty?

During puberty, shifts in mood can occur due to rising hormone levels. Sometimes “moodiness” can be a sign of depression, which may occur during puberty. For girls, negative self-image may develop as their bodies change, especially if they mature more slowly or more quickly than other kids their age.

## What else should I know?

When puberty begins before age 8 in girls or age 9 in boys, it may be “**central precocious puberty.**”



# What is central precocious puberty?

Central precocious puberty, or CPP, is the term for puberty that starts earlier than usual. That is, before age 8 in girls or age 9 in boys. CPP can even begin in infancy. The condition occurs in 1 out of every 5000 to 10,000 children,<sup>1</sup> and is much more common in girls than in boys (10 to 1).<sup>2</sup>

In most cases, the cause of CPP is unknown. But whatever the cause, the signs are the same as for “normal” puberty: breast development (and, rarely, menstruation) begins in girls, while the penis and testicles enlarge and develop in boys.

## Other signs may include:

- Appearance of pubic and underarm hair
- Sudden growth spurt
- Acne/oily skin
- Facial hair and a deepening voice in boys
- Changes in mood—what people think of as “teen attitude” or adolescent moodiness



**References:** 1. Antoniazzi F, Zamboni G. Central precocious puberty: current treatment options. *Pediatr Drugs*. 2004;6(4):212-231.

2. Pinyerd B, Zipf WB. Puberty—timing is everything! *J Pediatr Nurs*. 2005;20(2):75-82.



## CPP starts in the brain

As you learned before, the hypothalamus sends the GnRH signal to the pituitary gland. Modern treatments for CPP are designed to tell the pituitary to ignore the GnRH signal. This ultimately decreases the production of sex steroids.

## CPP affects growth and height

As you know, children experience growth spurts during puberty, and CPP is no exception. This makes the decision of treating CPP an important matter. Although children with CPP may initially be taller than other kids their age, they may end up shorter because they do not get enough time to grow before puberty. Without treatment, these children may never reach their expected adult height.

## CPP impacts lives of parents and children

You may already have seen the impact of CPP on your child. Children with CPP may develop differently than kids their own age.<sup>1</sup> Teachers, family members, and other adults may also treat children with CPP differently. Fortunately, today's medicines can treat CPP—and reduce the potential of emotional and physical effects of CPP.<sup>1</sup> The first step is to consult your doctor and decide on how to treat your child's CPP.

## How is CPP diagnosed?

To learn whether your child has CPP, your pediatrician may refer you to a pediatric endocrinologist, a children's doctor who specializes in hormonal disorders. Think of the doctor as your partner in helping to evaluate your child and guide you with recommendations throughout this process.

## The doctor visit

Your doctor will start the visit with a complete medical history. This conversation will include questions about other family members. Your child will also receive a physical exam and have his or her height and weight measured.



There are other tests that can help your doctor determine whether your child has CPP. Your child may be given some or all of the following tests:

- **Hand/wrist x-rays** to reveal whether the bones have matured early
- **Blood tests** to check the levels of different hormones
- **GnRH stimulation test** to determine if the pituitary hormones are at pubertal levels
- **Pelvic and adrenal ultrasound** to assess the size of ovaries, testicles, and adrenals
- **Magnetic resonance imaging (MRI) or computer-assisted tomography (CAT) scans** of the head to determine whether the hypothalamus and pituitary gland are normal



## How is CPP treated?

Based on results from your visit and the tests, the doctor can determine whether your child has early puberty and, if so, what may be the cause. Some children have “secondary” CPP—that is, something other than the pituitary gland is causing the signs of puberty. For “secondary” CPP, the underlying problem can be diagnosed and treated, which is designed to halt early puberty. If your child has “true” CPP—meaning the early puberty isn’t caused by something else—your doctor will recommend appropriate treatment.

Treatment for CPP is usually provided using a medicine called a GnRH agonist. A GnRH agonist tells the pituitary to ignore the GnRH signal. This generally stops early puberty. Without an active GnRH signal, the pituitary stops sending hormones to the ovaries or testicles. In turn, the ovaries or testicles stop making sex hormones. Bone maturation may also slow down. This may allow your child to reach his or her predicted adult height.



There are 3 ways your child can get approved GnRH agonist therapy:

- **Once-yearly implant:** One way to get GnRH agonist medicine is from a small implant, called SUPPRELIN® LA (histrelin acetate) subcutaneous implant, which lasts for a full year
- **Daily or monthly injection:** Although injection therapy may be given as frequently as once a day, the most common regimen is once a month. The injection must be given on a regular monthly schedule; otherwise, your child will restart puberty. Less frequent dosing regimens (for example, every 3 months) are not currently FDA-approved to treat children with CPP.
- **Multiple-times-daily nasal spray:** This therapy must be administered either 2 or 3 times a day. Each dose consists of 2 or 3 sprays per nostril, for a total of 8 to 9 sprays each day

Your child's doctor should do tests to make sure your child has CPP before treating with SUPPRELIN LA.

## What is SUPPRELIN® LA?

SUPPRELIN LA is a small, thin, flexible tube placed just under the skin of your child's inner upper arm. For a full year, SUPPRELIN LA continuously releases a steady flow of GnRH agonist medicine (known as histrelin). SUPPRELIN LA brings down sex hormone levels and keeps them down for one full year.

### How does my child get the implant?

SUPPRELIN LA will be prescribed by your pediatric endocrinologist and then inserted by a healthcare professional, such as a pediatric or general surgeon or your pediatric endocrinologist. The doctor will discuss how to make your child comfortable during the procedure. The doctor will temporarily numb your child's upper arm, make a small incision, and then place SUPPRELIN LA under the skin. The incision will then be closed with stitches or surgical strips and then covered with a bandage.



## Is there any special care I should give after the implant is in?

Do not remove the bandage for at least 24 hours to help ensure that the incision heals properly. While bandaged, your child should keep the arm clean and dry and should not swim or bathe. Do not remove the surgical strips. They will fall off on their own in several days, and always follow your healthcare professional's advice.

## When can my child go back to his or her normal activities?

For the first 7 days, your child should avoid heavy play or exercise. After the incision has healed, your child can resume normal activities. Your doctor will give you complete instructions.

## Will my child need follow-up care?

While SUPPRELIN LA is in place, your child should have regular visits with your pediatric endocrinologist. The doctor will perform regular exams and blood tests to check for signs of puberty; height and weight will be measured, and wrist x-rays may be taken to track bone growth.

Please see accompanying full Prescribing Information.



## What happens when the medicine in the implant runs out?

After a year, the implant should be removed. A new implant can be inserted, often in the same place, to continue treatment if you and your doctor decide continued treatment is required. In a research study, almost all (32 out of 33, or 97%) of the families of children who got SUPPRELIN® LA for 1 year chose to have another one put in when their doctor said the children still needed treatment.<sup>3</sup>

## When is the medicine stopped?

SUPPRELIN LA can be removed at any time. Your child's doctor will determine the right time to end treatment so puberty can begin again. This is usually before age 11 for girls and before age 12 for boys.





## Does SUPPRELIN LA have side effects?

In the first few weeks of treatment, like all GnRH agonist medicines, SUPPRELIN LA can cause a temporary increase in sex hormones. During this time, you may notice more signs of puberty in your child, including some vaginal bleeding and breast enlargement in girls. Within 4 weeks after treatment is started, you should see signs that puberty is stopping. Your doctor can further explain this to you.

The most common side effects of SUPPRELIN LA are skin reactions where the implant has been placed. Such reactions may include bruising, soreness, pain, tingling, itching, and swelling. They usually go away within 2 weeks on their own. Call the doctor if your child has bleeding, redness, or pain at the implant site. These may not be all the side effects of SUPPRELIN LA. Ask your doctor for more information.

**Reference: 3.** 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 Endocrin Metab.* 2007;92(5):1697-1704

Please see accompanying full Prescribing Information.



## How can I help my child handle CPP?

Just talking to your child can make a big difference. It may help if you explain what's happening to his or her body. Let your child know that puberty is a normal process that everyone goes through in life. It's just that, for some, puberty happens earlier.

If your child is being teased or bullied, try to get him or her to talk about it with you or with a teacher. It's also important to remind family members and other adults who know your child to treat your child according to his or her real age, no matter how old your child looks.

### Where can I get more information about CPP?

The following websites are good sources of information about CPP and other health issues that affect children. Remember, it's always best to talk personally with your child's doctor and other healthcare professionals.

#### The SUPPRELIN® LA website [www.supprelinla.com](http://www.supprelinla.com)

The SUPPRELIN LA website offers valuable resources and information about central precocious puberty (CPP) and treatment with SUPPRELIN LA.

From the first possible signs of early puberty in your young child all the way through diagnosis and treatment, this site contains in-depth information that can be helpful for you.

Please visit our Interactive Family Experience Videos, where you will see and hear other parents talk about their own experiences with CPP.



**Lawson Wilkins Pediatric Endocrine Society** [www.lwpes.org](http://www.lwpes.org)

LWPES is dedicated to the research and treatment of endocrine disorders and provides continuing education to its membership.

**The Magic Foundation** [www.magicfoundation.org](http://www.magicfoundation.org)

Major Aspects of Growth in Children (MAGIC) is a national nonprofit organization that provides support services for families whose children have growth hormone deficiency, or CPP.

**The Mayo Clinic** [www.mayoclinic.com](http://www.mayoclinic.com)

The Mayo Clinic website provides reliable health information on many diseases and conditions, drugs, treatment decisions, and much more.

**Web MD** [www.webmd.com](http://www.webmd.com)

Web MD offers expert, comprehensive information covering a wide variety of wellness and lifestyle issues, diseases, and conditions, plus physician and hospital locations.

**The CARES Foundation** [www.caresfoundation.org](http://www.caresfoundation.org)

The CARES Foundation offers personal support, educational conferences, newsletters, and a physician referral service.



SUPPRELIN® LA (histrelin acetate) implant is used for the treatment of children with central precocious puberty (CPP).

## Important Safety Information

SUPPRELIN LA should not be used by women who are or may become pregnant, and in patients who are allergic to gonadotropin releasing hormone (GnRH) or GnRH agonist analogs. Safety and effectiveness in children under 2 years of age has not been determined.

SUPPRELIN LA, like other GnRH agonists, may cause a temporary increase in the blood levels of specific hormones associated with the onset of puberty (estrogen in girls and testosterone in both sexes) during the first week of treatment. This increase may temporarily worsen puberty symptoms during the first week, additionally, you may see new symptoms appear during this period. Within the 4 weeks of treatment with SUPPRELIN LA, hormonal suppression generally occurs and the physical signs of puberty should decrease.

Your doctor should monitor the levels of specific hormones associated with puberty progression, 1 month after starting SUPPRELIN LA and then every 6 months thereafter. Every 6-12 months, height and bone age should also be monitored by your doctor.

During the clinical trial testing of SUPPRELIN LA, the most common side effects involved the implant site and included temporary bruising, pain, soreness, redness of the skin and swelling.

**Please talk with your doctor for more information or if you have any questions.**



R<sub>x</sub> only

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PHARMACEUTICALS

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