THE CAREGIVER'S GUIDE TO HELP KEEP TIME **ON THEIR SIDE**

Triptodur®
(triptorelin)
for extended release injectable suspension

Inside this handy guide you'll find more information about **central precocious puberty** and learn about a potential treatment option called Triptodur. You'll also find helpful resources on **how to support your child** during treatment.

IMPORTANT SAFETY INFORMATION FOR TRIPTODUR

INDICATION

TRIPTODUR is indicated for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP).

IMPORTANT SAFETY INFORMATION

Do not use TRIPTODUR in:

- Those allergic to gonadotropin releasing hormone (GnRH), GnRH agonist medicines, or any ingredients in TRIPTODUR.
- children under 2 years of age
- women who are or may become pregnant

Tell your child's healthcare provider if any of the above conditions apply to your child.

Please see additional Important Safety Information on page 8 and accompanying Full Prescribing Information.

What is **CPP**?

IMPORTANT SAFETY INFORMATION (CONT.)

It is important to stick to the dosing schedule (one injection every 24 weeks) in order for the drug to work. Do not miss or delay a scheduled dose.

Some people taking gonadotropin releasing hormone (GnRH) agonists like TRIPTODUR have had new or worsened mental (psychiatric) problems. Mental (psychiatric) problems may include emotional symptoms such as crying, irritability, restlessness (impatience), anger, or acting aggressive. Call your child's doctor right away if your child has any new or worsening emotional symptoms while taking TRIPTODUR.

Please see additional Important Safety Information on page 8 and accompanying Full Prescribing Information.

WHEN A NATURAL PROCESS **HAPPENS TOO SOON**

Puberty is a normal part of growing up. For some children, puberty can start too early. When this happens, it may be due to a condition called **central precocious puberty (CPP)**.

CPP occurs when a child shows signs of puberty sooner than normal.[1,2]

Before age 8 in girls

Before age 9 in boys

CPP is a rare condition that affects

1 in 5,000-10,000

children.[3]

If you suspect your child has CPP, it's probably because you've noticed changes in your child's physical development that seem to be happening sooner than they should. This might leave you feeling confused or stressed. It's important to know that there is power in information. Explore this guide to better understand the causes of CPP, the potential symptoms and effects, and a potential treatment option.

CPP **CAUSES AND DIAGNOSIS**

Although the exact cause is usually unknown, CPP results from the early release of a hormone from the brain called gonadotropin-releasing hormone (GnRH), which causes a child to begin puberty at an age earlier than normal.[4,5]

A pediatric endocrinologist is a type of physician who specializes in diagnosing, treating and managing disorders involving hormones, including CPP. If CPP is suspected, your pediatric endocrinologist will evaluate your child, and may order further testing. Some of those tests could include:[4]

- Blood tests to measure hormone levels, including a test called a GnRH stimulation test. In children with CPP, GnRH will cause other hormone levels in the body to rise. In children without CPP, these hormone levels will stay the same.
- An x-ray of the hand and wrist to measure how fast your child's bones are growing (often called a bone age test or study).
- An MRI (magnetic resonance imaging) or CT (computed tomography), which is a scan of the brain that looks to see whether any brain abnormalities are causing puberty to start too soon.

Treating **CPP**

The good news is that there is **treatment for CPP**. Below are some reasons why you and your child's physician may choose to **move forward with treatment**:

Growth and Height

- Your child may have experienced a growth spurt, related to CPP, and may even be tall for his or her age. Treatments for CPP are designed to delay puberty by stopping the signaling of certain hormones that are responsible for jump-starting the puberty process.[2]
- Children with CPP can be taller than their peers, however children that go **untreated may be shorter in height when they become adults**. This is because their growth plates (growth plates are areas of cartilage at the ends of long bones) close too early.[6] Typically, growth plates close toward the end stages of puberty.

Social and Emotional Impacts

- Girls and boys who begin puberty before their peers may be extremely self-conscious about the changes occurring in their bodies. This may affect their self-esteem and may increase their risk of developing depression, eating disorders, or substance abuse, perhaps as a result of standing out before they're ready for the extra attention.[4,7-9]

There are no data demonstrating outcome of Triptodur® on stature or social or emotional health.

IMPORTANT SAFETY INFORMATION (CONT.)

Some people taking GnRH agonists like TRIPTODUR have had seizures. The risk of seizures may be higher in people who have a history of seizures, have a history of epilepsy, have a history of brain or brain vessel (cerebrovascular) problems or tumors, are taking a medicine that has been connected with seizures such as bupropion or selective serotonin reuptake inhibitors (SSRIs). Seizures have also happened in people who have not had any of these problems. Call your child's doctor right away if your child has a seizure while taking TRIPTODUR.

What is **Triptodur®** (triptorelin)?

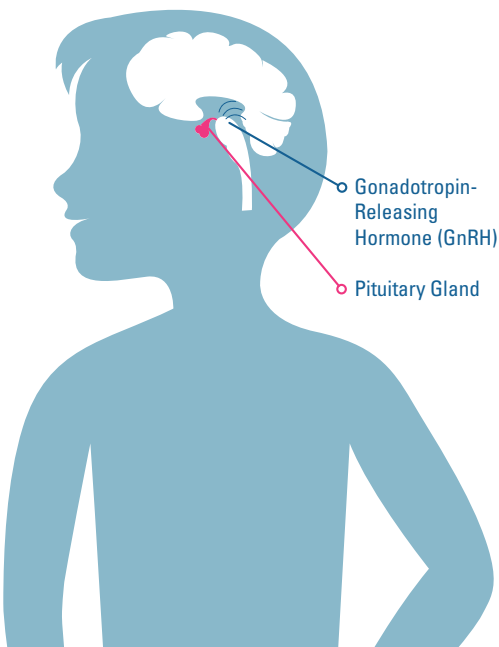
CENTRAL PRECOCIOUS PUBERTY (CPP) CAN BE TREATED **WITH TRIPTODUR**

Triptodur is an injectable prescription medicine used for the treatment of children 2 years of age or older with **central precocious puberty (CPP)**.[10] It is administered as a single intramuscular (IM) injection just once every 24 weeks, making it the **first FDA-approved medicine** for CPP to offer once-every six-month dosing. Treatment with Triptodur does not require surgery.

HOW CAN TRIPTODUR **HELP MY CHILD**?

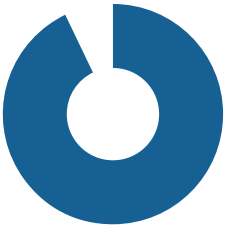
To understand how Triptodur works, it helps to know a little about what causes puberty. The process of puberty starts in the brain with the creation of a hormone called gonadotropin-releasing hormone (GnRH). GnRH causes the pituitary gland — a small bean-shaped gland at the base of the brain — to release two more hormones called luteinizing hormone (LH) and follicle-stimulating hormone (FSH). LH and FSH are involved in the growth and development of female and male sexual characteristics.[5]

Treatments for CPP weaken the effects of GnRH signaling on the pituitary gland, reducing the release of hormones that cause puberty. By stopping the signaling of these hormones, the puberty process will be delayed until the end of the treatment. The effect of Triptodur on pituitary and gonadal function is expected to disappear within six to twelve months after treatment is stopped.[10]

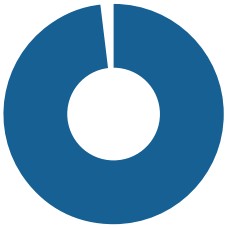


Triptodur® is effective in suppressing luteinizing hormone (LH) to prepubertal levels (≤5 IU/L).

In a phase III clinical trial,



93%
of patients
receiving Triptodur had their LH suppressed to prepubertal levels at **month six (primary endpoint)**, and



98%
of patients
maintained these levels at **12 months**.[10]

Triptodur was also found to be **well tolerated** with no unexpected side effects[10,11]

Benefits of Triptodur include:

Given only **twice a year** as an intramuscular injection[10]

Well tolerated therapy[10,11]

No surgery required

Long-lasting LH suppression[10,11]

WHAT TO EXPECT DURING TREATMENT

Triptodur must be administered under the supervision of a physician. It is important to stick to the dosing schedule (one injection every 24 weeks) in order for the medicine to work. Do not miss or delay a scheduled dose.[10]

Your child should have regular visits with his or her pediatrician or pediatric endocrinologist while undergoing treatment for CPP. Your child may need blood tests beginning 1 to 2 months following the start of treatment, during treatment as necessary to confirm efficacy, and with each subsequent dose.

During your child's treatment, a healthcare professional will perform regular exams and blood tests to check for signs of puberty, measure height and weight, and may take wrist X-rays to track bone growth.

The most common side effects of Triptodur include injection site reactions, menstrual (vaginal) bleeding, hot flush, headache, cough, and infections (bronchitis, gastroenteritis, influenza, nasopharyngitis, otitis externa, pharyngitis, sinusitis, and upper respiratory tract infection). Tell your child's healthcare provider if they have any side effect that bothers them or that does not go away.

These are not all the possible side effects of Triptodur. For more information, ask your child's healthcare provider or see the Important Safety Information for more details.

Please see additional Important Safety Information on page 8 and accompanying Full Prescribing Information.

IMPORTANT SAFETY INFORMATION (CONT.)

Some people taking triptorelin, the active ingredient in TRIPTODUR, have had serious allergic reactions. Call your child's doctor or get emergency medical help right away if your child gets any of the following symptoms of a serious allergic reaction: skin rashes, redness, or swelling, severe itching, hives, trouble breathing or swallowing, fast heartbeat, sweating, throat tightness, hoarseness, swelling of face, mouth, and tongue, dizziness or fainting.

Triptodur®
(triptorelin)
for extended release injectable suspension

IMPORTANT SAFETY INFORMATION FOR TRIPTODUR

TRIPTODUR® (triptorelin) for extended-release injectable suspension,for intramuscular use

INDICATION

TRIPTODUR is indicated for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP).

IMPORTANT SAFETY INFORMATION

Do not use TRIPTODUR in:

- Those allergic to gonadotropin releasing hormone (GnRH), GnRH agonist medicines, or any ingredients in TRIPTODUR.
- children under 2 years of age
- women who are or may become pregnant

Tell your child's healthcare provider if any of the above conditions apply to your child.

It is important to stick to the dosing schedule (one injection every 24 weeks) in order for the drug to work. Do not miss or delay a scheduled dose.

Some people taking gonadotropin releasing hormone (GnRH) agonists like TRIPTODUR have had new or worsened mental (psychiatric) problems. Mental (psychiatric) problems may include emotional symptoms such as crying, irritability, restlessness (impatience), anger, or acting aggressive. Call your child's doctor right away if your child has any new or worsening emotional symptoms while taking TRIPTODUR.

Some people taking GnRH agonists like TRIPTODUR have had seizures. The risk of seizures may be higher in people who have a history of seizures, have a history of epilepsy, have a history of brain or brain vessel (cerebrovascular) problems or tumors, are taking a medicine that has been connected with seizures such as bupropion or selective serotonin reuptake inhibitors (SSRIs). Seizures have also happened in people who have not had any of these problems. Call your child's doctor right away if your child has a seizure while taking TRIPTODUR.

Some people taking triptorelin, the active ingredient in TRIPTODUR, have had serious allergic reactions. Call your child's doctor or get emergency medical help right away if your child gets any of the following symptoms of a serious allergic reaction: skin rashes, redness, or swelling, severe itching, hives, trouble breathing or swallowing, fast heartbeat, sweating, throat tightness, hoarseness, swelling of face, mouth, and tongue, dizziness or fainting.

The most common side effects of TRIPTODUR include injection site reactions, menstrual (vaginal) bleeding, hot flush, headache, cough, and infections (bronchitis, gastroenteritis, influenza, nasopharyngitis, otitis externa, pharyngitis, sinusitis, and upper respiratory tract infection). These are not all the possible side effects of TRIPTODUR. Tell your child's healthcare provider if they have any side effect that bothers them or that does not go away.

In the first few weeks after your child receives their first TRIPTODUR injection or after additional injections, TRIPTODUR can cause a brief increase in some hormones. During this time you may notice more signs of puberty in your child, including vaginal bleeding. Call your child's doctor if signs of puberty continue after 2 months of receiving TRIPTODUR.

Reports of pseudotumor cerebri (idiopathic intracranial hypertension) have been observed in pediatric patients receiving GnRH agonists, including triptorelin. Patients and caregivers should contact their healthcare provider if the patient develops any of following symptoms of pseudotumor cerebri, including headache, and vision issues such as blurred vision, double vision, loss of vision, pain behind the eye or pain with eye movement, ringing in the ears, dizziness, and nausea.

These are not all the possible side effects of TRIPTODUR. Call your doctor for medical advice about side effects.

To report SUSPECTED ADVERSE REACTIONS, contact Azurity Pharmaceuticals, Inc. at 1-800-461-7449, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

The Important Safety Information does not include all the information needed to use TRIPTODUR safely and effectively. For additional safety information, please consult the full Prescribing Information for TRIPTODUR.

Please see additional Important Safety Information on page 8 and accompanying Full Prescribing Information.

IMPORTANT SAFETY INFORMATION (CONT.)

The most common side effects of TRIPTODUR include injection site reactions, menstrual (vaginal) bleeding, hot flush, headache, cough, and infections (bronchitis, gastroenteritis, influenza, nasopharyngitis, otitis externa, pharyngitis, sinusitis, and upper respiratory tract infection). These are not all the possible side effects of TRIPTODUR. Tell your child's healthcare provider if they have any side effect that bothers them or that does not go away.

In the first few weeks after your child receives their first TRIPTODUR injection or after additional injections, TRIPTODUR can cause a brief increase in some hormones. During this time you may notice more signs of puberty in your child, including vaginal bleeding. Call your child's doctor if signs of puberty continue after 2 months of receiving TRIPTODUR.

Guiding your child through treatment

KEEPING TRACK OF YOUR **CHILD'S GROWTH**

When you bring your child in for their regular doctor visits during treatment, it is helpful to report to the doctor any changes you see in your child's body such as: height, growth of underarm and pubic hair, breast development, voice change, and oily skin and acne.

Aside from the classic pencil markings on the doorway, there are other fun, interactive ways to track your child's body changes. Below are some ideas to make tracking your child's body changes less clinical, and more fun!

ART PROJECT

Create a giant ruler or use blank measuring tape with your child that you can use to track body changes, but there's also plenty of room to create fun designs and drawings together!

PHOTOSHOOT

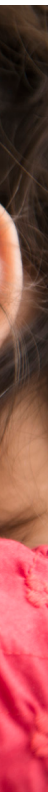
Let your child go to the store and pick out some of their favorite accessories. These accessories can be anything such as tiaras, scarves, a superhero costume, etc. Do regular "photoshoots" with your child using the same accessories and clothing items to track how fast they are outgrowing the items. You'll be able to track your child's growth and have some great photos for your memories!

Talking to Your Child About CPP: A Helpful Guide

Going through puberty too early can be a confusing and unsettling time for a child and his or her family. There are changes taking place in your child's body that he or she may not fully understand.[9]

As a parent, you play a key role in helping your child understand central precocious puberty (CPP). Creating a loving, comforting, and reassuring environment may help your child grow up to be strong and secure.[12]

This guide includes some helpful tips to keep in mind as you discuss CPP with your child.



FOR CHILDREN **AGES 3-6**:

Tip #1: Communication. Reinforce that your child's body is normal.

At such a young age, your child might not be fully aware of the changes happening in his or her body, and may even seem unaffected by it. However, children may ask questions about why they are going to the doctor, or why they have to get tests or treatment. If your child is tall or perhaps more developed for their age, he or she may also have other children or adults comment or ask questions about their growth.

How you talk about CPP can go a long way toward shaping your child's understanding of it, so it is a good idea to think about how you will discuss CPP with your child. It may be helpful to start with something like: "Everyone's body goes through these changes. Your body just started a little early."

It may also be helpful to use objects to open lines of communication between you and your child about the changes in his or her body. Comparing the size of objects such as toys gives children a chance to play with measurement and helps them learn how to compare and use words such as "taller," "shorter," etc.[13] For example, directly compare the heights of two stuffed toys and describe one toy as taller/shorter. This not only helps children understand measurement, but can help guide the conversation between you and your child about which parts of his or her body is growing or changing.

Tip #2. Prepare yourself so you can best help your child.

A CPP diagnosis can raise a lot of questions such as: What's happening to my child's body? Who do I talk to if I need help? Do I tell my friends and family?

Children often mimic their parent's behavior—your child is more likely to be anxious if you exhibit signs of stress.[14] Understanding CPP, and how you plan to talk with your child, family members, and even your doctors, can empower you to be a reliable support system for your child.

A simple explanation of CPP that can be used with friends and family is "My child has started puberty sooner than normal."

By talking to your child's doctor about CPP and what to expect, you can help ease your own uncertainties and anxieties.

Tip #3. Treat them according to their age.

Although your child's body is developing early, he or she is still a young child. Sometimes adults or other children may treat your child as if they are older because of their appearance.[9] If you are worried about family members, teachers, or other adults in your child's life treating him or her as if they are older, it may be helpful to explain the condition to them. Talk to your healthcare provider for suggestions on explaining CPP or share this helpful guide.

FOR CHILDREN **AGES 7 AND UP**:

Tip #1: Stay positive. Reinforce that your child is going through a natural process that usually happens at a later age.[6]

Right now, your child might not understand the changes happening in his or her body and may have negative feelings about developing early. How you talk about CPP can go a long way toward shaping your child's understanding of it. When discussing CPP, it is helpful to be open and honest about the changes happening to your child's body.[15] You can start out by saying something like: "Everybody goes through puberty. You just started a little early."

Tip #2. Prepare your child for what to expect.

Being diagnosed with CPP can raise a lot of questions such as: What's happening to my body? Why am I moody? Why don't I look like my friends?[9] By talking to your child about what CPP is and what to expect from it, you can help ease his or her fears and anxieties. Enlist the help of your child's health care providers to explain what is happening. Be sure to stay involved.

Tip #3. Be there.

Although your child's body is developing early, he or she is still a child and needs your support and guidance. Reassure your child that you're there when he or she has questions, concerns, or just wants to talk. It may be helpful to tell your child: "I'm here to help you" or "You can ask me anything."[9]

Tip #4: Help your child feel comfortable responding to questions.

Because it's natural for other people—especially kids—to be curious, it helps to arm your child with some simple responses to questions he or she may get from other kids. A confident, straightforward response to other people's curiosity can help.[15]

For example, if one of your daughter's classmates asks her why she has breasts, you may want to suggest that she smile and say, "Because I'm a girl." Or your child might choose a more direct approach and simply answer: "I have a medical condition" and leave it at that. The important thing is for your child not to feel ashamed or embarrassed about CPP.[9]

Children look for guidance on how to think about and respond to CPP. Your love and support means everything and can go a long way to boosting your child's self-acceptance.[9]

Please see additional Important Safety Information on page 8 and accompanying Full Prescribing Information.

IMPORTANT SAFETY INFORMATION (CONT.)

To report SUSPECTED ADVERSE REACTIONS, contact Azurity Pharmaceuticals, Inc. at **1-800-461-7449**, or FDA at **1-800-FDA-1088** or **www.fda.gov/medwatch**

The Important Safety Information does not include all the information needed to use TRIPTODUR safely and effectively. For additional safety information, please consult the full Prescribing Information for **TRIPTODUR**.

Please see additional Important Safety Information on page 8 and accompanying Full Prescribing Information.

Caregiver Resources

TRIPTODUR® IS WITH YOU **EVERY STEP OF THE WAY** THROUGH TREATMENT.

Triptodur provides parents and caregivers with **comprehensive support services** with the Triptodur Care Program.

Insurance, co-pays, and benefits can be difficult to navigate. The Triptodur Care Program offers you support before, during, and after treatment.

Copay Savings Program

Dedicated and Trained Staff

Benefits and Insurance Support

To learn more about the Triptodur Care Program and co-pay support, call us toll free at **833-401-CARE** or visit **www.triptodur.com**.

BELOW ARE SOME **ORGANIZATIONS AND RESOURCES** FOR **PARENTS AND CAREGIVERS** CARING FOR A CHILD WITH CENTRAL PRECOCIOUS PUBERTY (CPP).

HUMAN GROWTH FOUNDATION

The Human Growth Foundation leads the way in providing research, education, support, and advocacy in areas of growth or growth-hormone disorders. http://hgfound.org/

MAGIC FOUNDATION

The MAGIC Foundation is the world's largest organization for children and adults with growth-related disorders. https://www.magicfoundation.org/

Triptodur®
(triptorelin)
for extended release injectable suspension

REFERENCES

1. Muir A. Precocious Puberty. Pediatr Rev. 2006;27:373-381.
2. Carel JCm Léger J. Clinical Practice. Precocious puberty. N Engl J Med. 2008;358(22):2366-2377.
3. Partsch CJ, Sippell WG. Treatment of central precocious puberty. Best Pract Res Clin Endocrinol Metab.2002;16:165-189.
4. Precocious Puberty. Mayo Clinic Web site. http://www.mayoclinic.org/diseases-conditions/precocious-puberty/symptoms-causes/dxc-20266003. Accessed February 13, 2020.
5. What causes normal puberty, precocious puberty, & delayed puberty?. Eunice Kennedy Shriver National Institute of Child Health and Human Development Web site. https://www.nichd.nih.gov/health/topics/puberty/conditioninfo/Pages/causes.aspx. Accessed February 13, 2020.
6. Carel JC, Lahlou N, Roger M & Chaussain JL. Precocious puberty and statural growth. Human Reproduction Update. 2004;10:135-147.
7. Mendle, J., et al. Detrimental Psychological Outcomes Associated with Early Pubertal Timing in Adolescent Girls. Dev Rev. 2007; 27(2): 151-171.
8. Johansson T & Ritzen EM. Very long-term follow-up of girls with early and late menarche. Endocrine Development. 2005;8:126-136.
9. Helping your child cope with precocious puberty. WebMD website. Available at: https://www.webmd.com/parenting/features/helping-your-child-cope#3. Accessed February 13, 2020.
10. Triptodur [package insert]. Atlanta, GA: Arbor Pharmaceuticals, LLC.
11. Klein K, et al. Efficacy and safety of triptorelin 6-month formulation in patients with central precocious puberty. J Pediatr Endocrinol Metab. 2016;29(11):1241-1248.
12. Department For Children, Schools, And Families. Child Development Overview. (2017). Retrieved from: http://www.keap.org.uk/documents/eyfs_cards_0001207.pdf. Accessed on February 13, 2020.
13. MacDonald, A., & Lowrie, T. (2011). Developing measurement concepts within context: Children's representations of length. Mathematics Education Research Journal, 23(1), 27–42. https://doi.org/10.1007/s13394-011-0002-7
14. Maccoby, E. E. (1992). The role of parents in the socialization of children: An historical overview. Developmental Psychology, 28(6), 1006.
15. Bordini, B. (2017). Precocious Puberty. The MAGIC Foundation. Retrieved from: https://www.magicfoundation.org/Downloads/Precocious%20Puberty%20final.pdf. Accessed on February 13, 2020.

NOTES

Triptodur®
(triptorelin)
for extended release injectable suspension

GROWING UP HAPPENS **FAST,** HELP KEEP TIME ON THEIR SIDE WITH **TRIPTODUR** (TRIPTORELIN)

arbor®
PHARMACEUTICALS, LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use TRIPTODUR® safely and effectively. See full prescribing information for TRIPTODUR.

TRIPTODUR (triptorelin) for extended-release injectable suspension, for intramuscular use
Initial U.S. Approval: 2000

----------RECENT MAJOR CHANGES----------
Warnings and Precautions (5.4) 04/2022

----------INDICATIONS AND USAGE----------
TRIPTODUR is a gonadotropin releasing hormone (GnRH) agonist indicated for the treatment of pediatric patients 2 years and older with central precocious puberty. (1)

----------DOSAGE AND ADMINISTRATION----------
- Must be administered under supervision of a physician. (2.1)
- Administer TRIPTODUR as a single intramuscular injection of 22.5 mg once every 24 weeks. (2.1)
- Monitor response with LH levels after a GnRH or GnRH agonist stimulation test, basal LH, or serum concentration of sex steroid levels beginning 1 to 2 months following initiation of therapy, during therapy as necessary to confirm maintenance of efficacy, and with each subsequent dose. (2.2)
- Measure height every 3-6 months and monitor bone age periodically. (2.2)
- See FPI for reconstitution and administration instructions. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
For extended-release injectable suspension: 22.5 mg of triptorelin as a powder cake for reconstitution with the co-packaged 2 mL of diluent Sterile Water for Injection. (3)

----------CONTRAINDICATIONS----------
- Hypersensitivity reactions (4)
- Pregnancy (4, 8.1)

----------WARNINGS AND PRECAUTIONS----------
- *Initial Rise of Gonadotropins and Sex Steroid Levels:* An increase in clinical signs and symptoms of puberty may be observed during the first 2-4 weeks of therapy since gonadotropins and sex steroids rise above baseline because of the initial stimulatory effect of the drug. (5.1)
- *Psychiatric events:* Have been reported in patients taking GnRH agonists. Events include emotional lability, such as crying, irritability, impatience, anger, and aggression. Monitor for development or worsening of psychiatric symptoms. (5.2)
- *Convulsions:* Have been observed in patients with or without a history of seizures, epilepsy, cerebrovascular disorders, central nervous system anomalies or tumors, and in patients on concomitant medications that have been associated with convulsions. (5.3)
- *Pseudotumor Cerebri (Idiopathic Intracranial Hypertension):* Have been reported in pediatric patients receiving GnRH agonists, including triptorelin. Monitor patients for headache, papilledema, and blurred vision. (5.4)

----------ADVERSE REACTIONS----------
In clinical trials for TRIPTODUR, the most common adverse reactions (≥4.5%) are injection site reactions, menstrual (vaginal) bleeding, hot flush, headache, cough, and infections (bronchitis, gastroenteritis, influenza, nasopharyngitis, otitis externa, pharyngitis, sinusitis, and upper respiratory tract infection). (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Arbor Pharmaceuticals, LLC at 1-866-516-4950 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 04/2022

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

TRIPTODUR is indicated for the treatment of pediatric patients 2 years of age and older with central precocious puberty (CPP).

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

TRIPTODUR must be administered under the supervision of a physician.

The dosage of TRIPTODUR is 22.5 mg reconstituted with accompanying diluent (Sterile Water) 2 mL, and administered as a single intramuscular injection once every 24 weeks.

TRIPTODUR treatment should be discontinued at the appropriate age of onset of puberty at the discretion of the physician.

2.2 Monitoring

Monitor response to TRIPTODUR with LH levels after a GnRH or GnRH agonist stimulation test, basal LH, or serum concentration of sex steroid levels beginning 1 to 2 months following initiation of therapy, during therapy as necessary to confirm maintenance of efficacy, and with each subsequent dose.

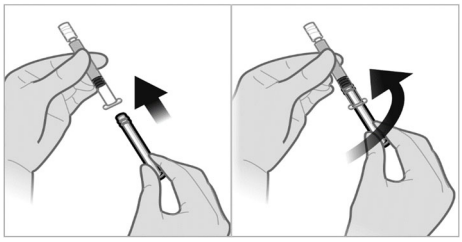
Measure height (for calculation of growth rate) every 3-6 months and monitor bone age periodically.

Noncompliance with drug regimen or inadequate dosing may result in inadequate control of the pubertal process with gonadotropins and/or sex steroids increasing above prepubertal levels. If the dose of TRIPTODUR is not adequate switching to an alternative GnRH agonist for the treatment of CPP with the ability for dose adjustment may be necessary.

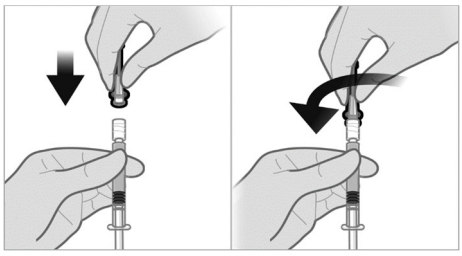
2.3 Reconstitution and Administration Instructions

Please read these instructions completely before you begin.

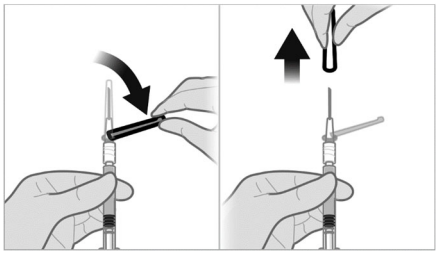
- Use appropriate aseptic technique for preparation and administration.
- Screw the plunger rod into the barrel end of the prefilled sterile water diluent syringe.



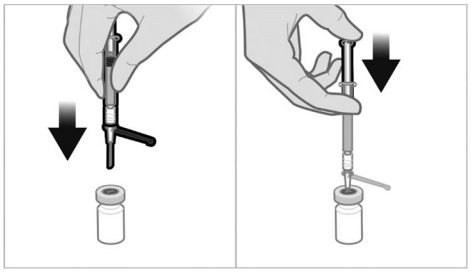
- Remove the cap from the syringe barrel.
- **Firmly attach** one of the 21-gauge sterile safety needles onto the prefilled sterile water diluent syringe with a push and clockwise twist. This 21-gauge needle will only be used for reconstitution of the product.



  - Pull back on the safety cover towards the syringe and away from the 21-gauge needle. Then pull the clear needle shield off.

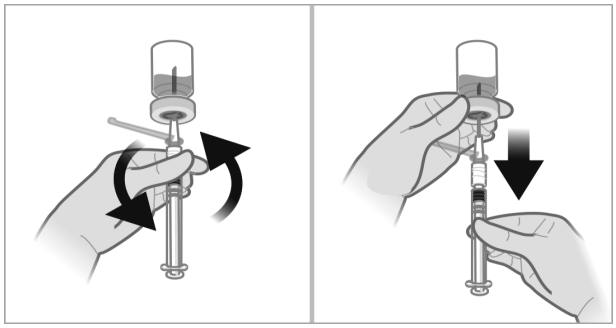


- Insert the 21-gauge needle to inject the Sterile Water diluent into the vial. Do not release the plunger rod. Gently swirl the vial ensuring the diluent rinses the sides of the vial. The reconstituted solution is a milky suspension.

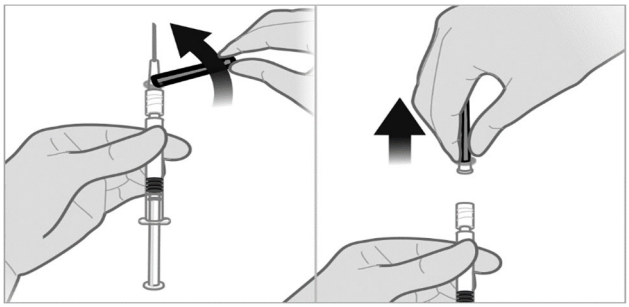


Important: Once mixed, proceed to the next steps and administer without delay.

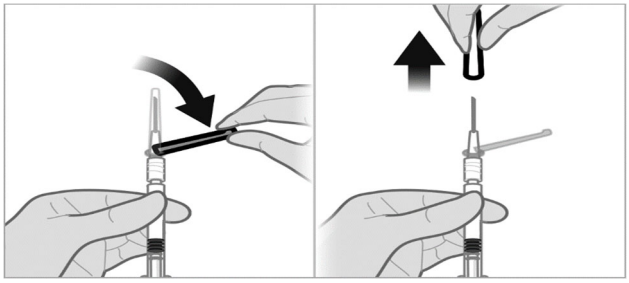
- Invert the vial and move back the syringe in order to position the end of the 21-gauge needle very near the level of the stopper, making sure the needle lumen is still completely in the vial.
- Pull back the plunger rod slowly to withdraw the reconstituted product into the syringe, withdrawing as much of the reconstituted product into the syringe as possible.



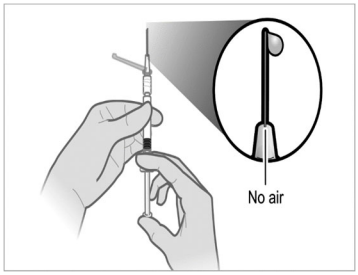
- Push the safety cover forward toward the needle until you hear and/or feel it lock. Then remove the first 21-gauge needle by grasping the needle hub to disconnect the needle from the syringe and discard it. **This (first) 21-gauge needle will no longer be used.**



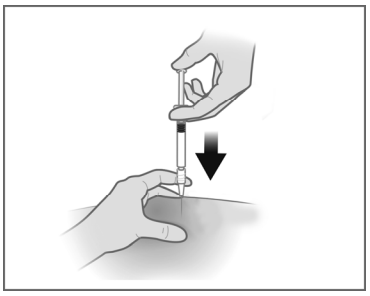
- **Firmly attach the *second* sterile needle** onto the syringe pull back the safety cover towards the syringe. This 21-gauge needle will be used for administration.



- Prime the 21-gauge needle to first remove air from the syringe, inspect the suspension visually for particulate matter and discoloration. If the suspension appears milky and homogenous without visible aggregates or precipitates then administer the suspension immediately.



- Inject the patient preferably in either buttock or thigh using the entire contents of the syringe.



- **The injection of the suspension should be performed relatively rapidly and in a steady and uninterrupted manner in order to avoid any potential blockage of the needle.**

After administering the injection, immediately activate the safety cover:

- Center your thumb or forefinger on the textured finger pad area of the safety cover and push it forward over the needle until you hear or feel it lock.
- Use the one-handed technique and activate the mechanism away from yourself and others.
- Immediately discard the syringe assembly into a suitable sharps container.

3 DOSAGE FORMS AND STRENGTHS

For extended-release injectable suspension: 22.5 mg of triptorelin as a lyophilized white to slightly yellow powder cake in a single-dose vial for reconstitution with the co-packaged 2 mL of diluent (Sterile Water) for Injection.

4 CONTRAINDICATIONS

- Hypersensitivity: TRIPTODUR is contraindicated in individuals with a known hypersensitivity to triptorelin, any other component of the product, or other GnRH agonists or GnRH *[see Adverse Reactions (6.2)]*.
- Pregnancy: TRIPTODUR may cause fetal harm *[see Use in Specific Populations (8.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Initial Rise of Gonadotropins and Sex Steroid Levels

During the early phase of initial therapy or after subsequent doses, gonadotropins and sex steroids may rise above baseline because of a transient stimulatory effect of the drug *[see Clinical Pharmacology (12.2)]*. Therefore, a transient increase in clinical signs and symptoms of puberty, including vaginal bleeding, may be observed during the first weeks of therapy or after subsequent doses.

5.2 Psychiatric Events

Psychiatric events have been reported in patients taking GnRH agonists, including triptorelin. Postmarketing reports with this class of drugs include symptoms of emotional lability, such as crying, irritability, impatience, anger, and aggression. Monitor for development or worsening of psychiatric symptoms during treatment with TRIPTODUR *[see Adverse Reactions (6)]*.

5.3 Convulsions

Postmarketing reports of convulsions have been observed in patients receiving GnRH agonists, including triptorelin. These 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 *[see Adverse Reactions (6)]*.

5.4 Pseudotumor Cerebri Idiopathic Intracranial Hypertension

Pseudotumor cerebri (idiopathic intracranial hypertension) has been reported in pediatric patients receiving GnRH agonists, including triptorelin. Monitor patients for signs and symptoms of pseudotumor cerebri, including headache, papilledema, blurred vision, diplopia, loss of vision, pain behind the eye or pain with eye movement, tinnitus, dizziness, and nausea.

6 ADVERSE REACTIONS

The following serious adverse reactions are described here and elsewhere in the label:

- Initial Rise of Gonadotropins and Sex Steroid Levels *[see Warnings and Precautions (5.1)]*
- Psychiatric Events *[see Warnings and Precautions (5.2)]*
- Convulsions *[see Warnings and Precautions (5.3)]*
- Pseudotumor Cerebri (Idiopathic Intracranial Hypertension) *[see Warnings and Precautions (5.4)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of TRIPTODUR was evaluated in one uncontrolled, open-label single-arm clinical trial in which 44 children with central precocious puberty received two doses of TRIPTODUR and were observed for 12 months. The median age of the study population was 8 years (range 2-9 years) at treatment start; 88.6% of subjects were female, 59.1% were White, 27.3% were Black and 4.5% were Asian. Table 1 shows all the adverse reactions that occurred in at least 2 patients (≥4.5%) during the open-label single-arm trial.

Table 1: Adverse Reactions[1] Occurring in ≥ 2 Patients Treated with TRIPTODUR in an Open-Label Single-Arm Trial

Adverse Reactions	Number of Patients Reporting Event (%) (Total N=44)
Infections & Infestations	
Bronchitis	2 (4.5)
Gastroenteritis	3 (6.8)
Influenza	2 (4.5)
Nasopharyngitis	6 (13.6)
Otitis externa	2 (4.5)
Pharyngitis	2 (4.5)
Sinusitis	2 (4.5)
Upper respiratory tract infection	4 (9.1)
Nervous System Disorders	
Headache	6 (13.6)
Reproductive System & Breast Disorders	
Menstrual (Vaginal bleeding)[2]	3 (7.7)
Respiratory, Thoracic & Mediastinal Disorder	
Cough	3 (6.8)
Vascular Disorders	
Hot flush	2 (4.5)

[1]Injection site reactions are presented separately
[2]Includes % of patients with vaginal bleeding or menstrual disorder ("menstrual cycle returned") in 39 females out of N=44.

Other Selected Adverse Reactions:

Injection Site Reactions

Injection site reactions occurring in patients immediately and/or 2 hours after injection include pain (45%), redness (14%), pruritus (2.3%) and swelling (2.3%).

Psychiatric Disorders

Anxiety (2.3%) and mood altered (2.3%)

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of triptorelin. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Hypersensitivity Reactions: Anaphylactic shock, anaphylactoid reaction, angioedema, urticaria.

Cardiovascular: Hypertension.

Psychiatric: Emotional lability, such as crying, irritability, impatience, anger, and aggression. Depression, including rare reports of suicidal ideation and attempt. Many, but not all, of these patients had a history of psychiatric illness or other comorbidities with an increased risk of depression.

Nervous System: Convulsions, pseudotumor cerebri (idiopathic intracranial hypertension)

Vision Disorders: Visual impairment, visual disturbance

7 DRUG INTERACTIONS

7.1 Drug-Drug Interactions

Results of *in vitro* studies show that drug-drug interactions with triptorelin are unlikely *[see Clinical Pharmacology (12.3)]*. However, in the absence of relevant data and as a precaution, hyperprolactinemic drugs should not be used concomitantly with triptorelin since hyperprolactinemia reduces the number of pituitary GnRH receptors.

7.2 Drug-Laboratory Test Interactions

Administration of TRIPTODUR results in suppression of the pituitary-gonadal system.

The effect of TRIPTODUR on pituitary and gonadal function is expected to disappear within six to twelve months after treatment discontinuation. Therefore, diagnostic tests of pituitary gonadotropic and gonadal functions conducted during treatment or after discontinuation of treatment may be affected.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

TRIPTODUR is contraindicated in women who are pregnant *[see Contraindications (4)]* since expected hormonal changes that occur with TRIPTODUR treatment increase the risk for pregnancy loss. Available data with triptorelin use in pregnant women are insufficient to determine a drug-associated risk of adverse developmental outcomes. Based on mechanism of action in humans and findings of increased pregnancy loss in animal studies, TRIPTODUR may cause fetal harm when administered to pregnant women. Advise pregnant women of the potential risk to a fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% - 4% and 15% -20%, respectively.

Data

Animal Data

In pregnant rats administered triptorelin at doses of 2, 10, and 100 mcg/kg/day during the period of organogenesis, maternal toxicity (decrease in body weight) and embryo-fetal toxicities (pre-implantation loss, increased resorption, and reduced number of viable fetuses) were observed at 100 mcg/kg, approximately 4 times the clinical dose based on body surface area. No embryonic and fetal developmental toxicities were observed in mice at doses up to 4 times the clinical dose. Teratogenic effects were not observed in viable fetuses in rats or mice.

8.2 Lactation

Risk Summary

There are no data on the presence of triptorelin in human milk, or the effects of the drug on the breastfed infant, or on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TRIPTODUR and any potential adverse effects on the breastfed child from TRIPTODUR or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of TRIPTODUR have been established in pediatric patients 2 years of age and older based on a single-arm open-label study of 44 children 2-9 years of age with CPP *[see Clinical Studies (14)]*. The safety and effectiveness of TRIPTODUR have not been established in pediatric patients less than 2 years old.

8.6 Renal Impairment

TRIPTODUR has not been studied in children with renal impairment. Adult subjects with renal impairment had higher exposure than young healthy adult males *[see Clinical Pharmacology (12.3)]*.

8.7 Hepatic Impairment

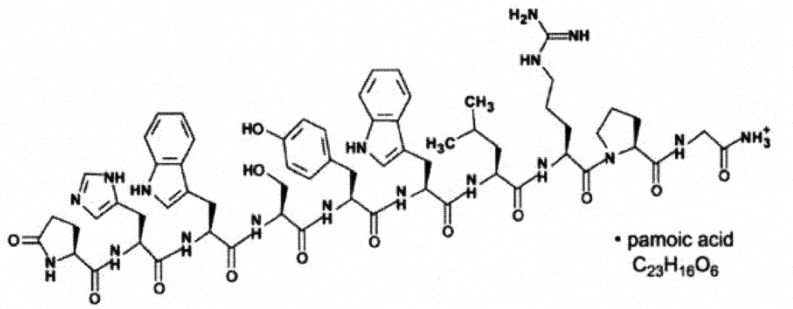
TRIPTODUR has not been studied in children with hepatic impairment. Adult subjects with hepatic impairment had higher exposure than young healthy adult males *[see Clinical Pharmacology (12.3)]*.

10 OVERDOSAGE

There is no experience with overdosage in clinical trials of triptorelin. If overdosage occurs, therapy should be discontinued and appropriate supportive and symptomatic treatment administered.

11 DESCRIPTION

TRIPTODUR contains the pamoate salt of triptorelin, a synthetic decapeptide analog of naturally occurring gonadotropin-releasing hormone (GnRH or LHRH). The chemical name of triptorelin pamoate is 5-oxo-L-prolyl-L-histidyl-L-tryptophyl-L-seryl-L-tyrosyl-D-tryptophyl-L-leucyl-L-arginyl-L-prolylglycine amide (pamoate salt). The molecular weight is 1699.9 and the structural formula is:



TRIPTODUR for extended release injectable suspension for intramuscular use is provided as a sterile, lyophilized, biodegradable microgranule formulation in a single-dose vial, co-packaged with a syringe containing 2 mL Sterile Water for Injection for reconstitution of the lyophilisate. The triptorelin formulation is comprised of 22.5 mg triptorelin (equivalent to 31 mg triptorelin pamoate), poly-*d,l*-lactide-co-glycolide (183 mg), mannitol (74 mg), carboxymethylcellulose sodium (26 mg), and polysorbate 80 (1.7 mg). When 2 mL Sterile Water for Injection is added to the vial containing TRIPTODUR and mixed, a suspension is formed which is intended as a single intramuscular injection.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Triptorelin is a GnRH agonist.

12.2 Pharmacodynamics

Following the first administration, there is a transient surge in circulating levels of LH, FSH, testosterone, and estradiol *[see Warnings and Precautions (5.2)]*. After chronic and continuous administration, by 4 weeks after initiation of therapy, a sustained decrease in LH and FSH secretion and marked reduction in sex steroids are observed.

12.3 Pharmacokinetics

Absorption
After an initial intramuscular TRIPTODUR 22.5 mg injection and a second 22.5 mg intramuscular injection 24 weeks later in children 2 to 9 years old with CPP, triptorelin peaked 4 hours postdose with a geometric mean C_{max} of 39.9 and 36.5 ng/mL, respectively. No apparent accumulation of triptorelin occurred after the second injection. Absorption occurred in two phases, a burst phase followed by a maintenance release phase. In children with CPP, following the burst phase after the first 22.5 mg injection, geometric mean serum triptorelin levels were 0.11, 0.17, 0.05 and 0.03 ng/mL at Months 1, 2, 3, and 6, respectively.

Distribution
There is no evidence that triptorelin, at clinically relevant concentrations, binds to plasma proteins.

Elimination

Metabolism
The metabolism of triptorelin in humans is unknown, but is unlikely to involve hepatic microsomal enzymes (cytochrome P450). Thus far no metabolites of triptorelin have been identified. Pharmacokinetic data suggest that C-terminal fragments produced by tissue degradation are either completely degraded in the tissues, or rapidly degraded in plasma, or cleared by the kidneys.

Excretion
Triptorelin is eliminated by both the liver and the kidneys. Following intravenous administration of 0.5 mg triptorelin peptide to six healthy male volunteers with a creatinine clearance of 149.9 mL/min, 41.7% of the dose was excreted in urine as intact peptide with a total triptorelin clearance of 211.9 mL/min. This percentage increased to 62.3% in patients with liver disease who have a lower creatinine clearance (89.9 mL/min). It has also been observed that the nonrenal clearance of triptorelin (patient anuric, $Cl_{creat} = 0$) was 76.2 mL/min, thus indicating that the nonrenal elimination of triptorelin is mainly dependent on the liver.

Specific Populations

Renal Impairment
After intravenous bolus injection of 0.5 mg triptorelin in adults, the two distribution half-lives were unaffected by renal impairment. However, renal insufficiency led to a decrease in total triptorelin clearance proportional to the decrease in creatinine clearance as well as increases in volume of distribution and consequently, an increase in the elimination half-life. Adult male subjects with moderate or severe renal impairment had approximately 2-fold higher exposure (AUC values) than young healthy adult males (see Table 1) *[see Use in Specific Populations (8.6)]*.

Hepatic Impairment
After intravenous bolus injection of 0.5 mg triptorelin in adults, the two distribution half-lives were unaffected by hepatic impairment. In adult males with hepatic insufficiency, triptorelin clearance was reduced and exposure (AUC) was increased 3.7-fold compared to young healthy adult males (Table 2) *[see Use in Specific Populations (8.7)]*.

Table 2: Pharmacokinetic Parameters (Mean ± SD) in Healthy Adults, Adults with Renal Impairment, and Adults with Hepatic Impairment Following an I.V. Bolus of 0.5 mg Triptorelin in Solution

Group	C_{max} (ng/mL)	AUC_{inf} (h·ng/mL)	Cl_p (mL/min)	Cl_{renal} (mL/min)	$t_{1/2}$ (h)	Cl_{creat} (mL/min)
6 healthy male volunteers	48.2 ±11.8	36.1 ±5.8	211.9 ±31.6	90.6 ±35.3	2.81 ±1.21	149.9 ±7.3
6 males with moderate renal impairment	45.6 ±20.5	69.9 ±24.6	120.0 ±45.0	23.3 ±17.6	6.56 ±1.25	39.7 ±22.5
6 males with severe renal impairment	46.5 ±14.0	88.0 ±18.4	88.6 ±19.7	4.3 ±2.9	7.65 ±1.25	8.9 ±6.0
6 males with liver disease	54.1 ±5.3	131.9 ±18.1	57.8 ±8.0	35.9 ±5.0	7.58 ±1.17	89.9 ±15.1

Drug-Drug Interactions

In Vitro Assessment of Drug Interactions

Drug Metabolizing Enzyme Inhibition
Triptorelin did not inhibit CYP1A2, 2B6, 2C8, 2C9, 2C19 or 2D6, or CYP 3A4/5 at clinically relevant concentrations.

Drug Metabolizing Enzyme Induction

In fresh human hepatocytes from three human donors, triptorelin did not induce CYP1A2 or CYP3A4/5 activity.

Transporters
Triptorelin was a poor P-gp substrate and had no inhibitory effect toward P-gp.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis was evaluated in an 18-month study in mice and a 24-month study in rats. In rats, triptorelin doses of 120, 600, and 3000 mcg/kg given every 28 days (approximately 0.2, 0.8, and 4 times the estimated human monthly dose based on body surface area) resulted in increased mortality with a drug treatment period of 13 to 19 months. The incidences of benign and malignant pituitary tumors and histosarcomas were increased in a dose-related manner. There were no treatment-related tumors in mice at exposure up to 4-fold higher than the estimated human monthly dose based on body surface area.

Mutagenicity studies performed with triptorelin using bacterial and mammalian systems (*in vitro* Ames test and chromosomal aberration test in CHO cells and an *in vivo* mouse micronucleus test) provided no evidence of mutagenic potential.

After 60 days of subcutaneous treatment followed by a minimum of four estrus cycles prior to mating, triptorelin at doses of 2, 20, and 200 mcg/kg (approximately 0.07, 0.7, and 7 times the estimated human daily dose based on body surface area) or two monthly injections as slow release microspheres (~20 mcg/kg/day) had no effect on the fertility or general reproductive function of female rats.

No studies were conducted to assess the effect of triptorelin on male fertility.

14 CLINICAL STUDIES

In a single-arm open-label study, 44 children 2 to 9 years of age with CPP, 39 females and 5 males, all naïve to previous GnRH agonist treatment, were administered TRIPTODUR 22.5 mg at a dosing interval of 24 weeks. Subjects were evaluated over two dosing intervals for a total of 12 months.

TRIPTODUR 22.5 mg suppressed pituitary release of LH and FSH and, consequently, gonadal secretion of estradiol in girls and testosterone in boys (Table 3). At all timepoints evaluated, ≥93% of children achieved LH suppression to prepubertal levels (i.e., serum LH ≤5 IU/L 30 minutes after GnRH agonist stimulation), ≥79% of girls achieved prepubertal levels of estradiol (i.e., <20 pg/mL), and ≥80% of boys achieved prepubertal levels of testosterone (i.e., <30 ng/dL). TRIPTODUR arrested or reversed progression of clinical signs of puberty with 95% of children showing no increase in the bone age/chronological age ratio, and 89% showing stabilization of sexual maturation at Month 12.

Table 3: Efficacy of TRIPTODUR 22.5 mg Administered Every 6 Months to Children with CPP[a]

Endpoint	% (n/N) of Children Achieving Endpoint					
	Month 1	Month 2	Month 3	Month 6	Month 9	Month 12
% with prepubertal LH (GnRH-stim LH ≤5 IU/L)	95% (42/44)	95% (42/44)	95% (42/44)	93%[b] (41/44)	95% (42/44)	98% (43/44)
% girls with prepubertal estradiol (<20 pg/mL)	87% (34/39)	89% (34/38)	92% (36/39)	79% (31/39)	82% (32/39)	79% (31/39)
% boys with prepubertal testosterone (<30 ng/dL)	80% (4/5)	80% (4/5)	100% (5/5)	100% (5/5)	80% (4/5)	80% (4/5)
% with no increase in BA/CA[c] ratio vs. baseline				64% (28/44)		95% (42/44)
% achieving stabilization of sexual maturation				91% (40/44)		89% (39/44)
% girls with regression of uterine length				69% (27/39)		77% (30/39)
% boys with no progression in testis volumes				100% (5/5)		100% (5/5)

a- Intent-to-Treat population
b- Primary efficacy endpoint
c- Bone Age/Chronological Age

Following the second TRIPTODUR injection, 22 children (all girls) were assessed for evidence of an acute-on-chronic phenomenon (i.e., increase in basal LH >5 IU/L or serum estradiol level >20 pg/mL 48 hours after the second triptorelin injection). Of these, one girl who achieved prepubertal hormone levels prior to the second injection showed biochemical evidence of acute-on-chronic phenomenon *[see Warnings and Precautions (5.2) and Adverse Reactions (6.1)]*.

16 HOW SUPPLIED/STORAGE AND HANDLING

Each TRIPTODUR 22.5 mg single-use kit (NDC 24338-150-20) contains:

- One single-dose vial of TRIPTODUR 22.5 mg (NDC 24338-150-01) with a Flip-Off seal containing sterile lyophilized white to slightly yellow powder cake
- One sterile, glass syringe with Luer Lock prefilled with 2 mL of Sterile Water for Injection (NDC 24338-150-02)
- Two sterile 21 gauge, 1½" needles (*thin-wall*) with safety cover
- One Package Insert

Store at 20-25°C (68-77°F) [see USP Controlled Room Temperature]. Do not freeze.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Medication Guide).

Hypersensitivity Reactions

Inform caregivers that anaphylactic shock, hypersensitivity, and angioedema have been reported with triptorelin use and to immediately seek medical attention if any hypersensitivity reaction occurs.

Symptoms after Initial TRIPTODUR Administration

Inform caregivers that during the first weeks after the first TRIPTODUR injection, signs of puberty may occur such as vaginal bleeding *[see Warnings and Precautions (5.1) and Adverse Reactions (6.1)]*. Caregivers should notify the physician if these symptoms continue beyond the second month after TRIPTODUR administration.

Psychiatric Events

Inform caregivers that symptoms of emotional lability, such as crying, irritability, impatience, anger, and aggression have been observed in patients receiving GnRH agonists, including triptorelin. Alert caregivers to the possibility of development or worsening of psychiatric symptoms, including depression, during treatment with TRIPTODUR *[see Warnings and Precautions (5.2) and Adverse Reactions (6.2)]*.

Convulsions

Inform caregivers that reports of convulsions have been observed in patients receiving GnRH agonists, including triptorelin. 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 may be at increased risk *[see Warnings and Precautions (5.3)]*.

Pseudotumor Cerebri (Idiopathic Intracranial Hypertension)

Inform patients and caregivers that reports of pseudotumor cerebri (idiopathic intracranial hypertension) have been observed in pediatric patients receiving GnRH agonists, including triptorelin. Monitor patients for signs and symptoms of pseudotumor cerebri, including headache, and vision issues such as blurred vision, double vision, loss of vision, pain behind the eye or pain with eye movement, ringing in the ears, dizziness, and nausea. Advise patients and caregivers to contact their healthcare provider if the patient develops any of these symptoms. *[see Warnings and Precautions (5.4)]*.

Pregnancy is Contraindicated

TRIPTODUR is contraindicated in pregnancy. If the patient becomes pregnant while taking the drug, the patient should be informed of the potential risk to fetus *[see Use in Specific Populations (8.1)]*.

Compliance with the Dosing Schedule

Inform caregivers about the importance of adherence to the TRIPTODUR dosing schedule of one injection every 24 weeks. Patients should not miss or delay a scheduled dose.

Manufactured for:
Arbor Pharmaceuticals, LLC
Atlanta, GA 30328

Manufactured by:
Debiopharm Research & Manufacturing SA
CH-1920 Martigny, Switzerland

TRIP-PI-06

MEDICATION GUIDE

TRIPTODUR® [TRIP-toe-der]

(triptorelin)

for extended-release injectable suspension, for intramuscular use

What is the most important information I should know about TRIPTODUR?

- In the first few weeks after your child receives their first TRIPTODUR injection or after additional injections, TRIPTODUR can cause a brief increase in some hormones. During this time you may notice more signs of puberty in your child, including vaginal bleeding. Call your child's doctor if signs of puberty continue after 2 months of receiving TRIPTODUR.
- Some people taking gonadotropin releasing hormone (GnRH) agonists like TRIPTODUR have had new or worsened mental (psychiatric) problems. Mental (psychiatric) problems may include emotional symptoms such as:
  - crying
  - irritability
  - restlessness (impatience)
  - anger
  - acting aggressive

Call your child's doctor right away if your child has any new or worsening emotional symptoms while taking TRIPTODUR.

- Some people taking GnRH agonists like TRIPTODUR have had seizures. The risk of seizures may be higher in people who:
  - have a history of seizures
  - have a history of epilepsy
  - have a history of brain or brain vessel (cerebrovascular) problems or tumors
  - are taking a medicine that has been connected with seizures such as bupropion or selective serotonin reuptake inhibitors (SSRIs)

Seizures have also happened in people who have not had any of these problems.

Call your child's doctor right away if your child has a seizure while taking TRIPTODUR.
Increased pressure in the fluid around the brain can happen in children taking GnRH agonists medicines including TRIPTODUR.

• Call your child's doctor right away if your child has any of the following symptoms during treatment with TRIPTODUR:

- headache
- eye problems, including blurred vision, double vision and decreased eyesight
- eye pain
- ringing in the ears
- dizziness
- nausea

What is TRIPTODUR?

- TRIPTODUR is an injectable prescription GnRH medicine used for the treatment of children with central precocious puberty (CPP).
- It is not known if TRIPTODUR is safe and effective in children under 2 years of age.

TRIPTODUR should not be taken if your child is:

- allergic to gonadotropin releasing hormone (GnRH), GnRH agonist medicines, or any ingredients in TRIPTODUR. See the end of this Medication Guide for a complete list of ingredients in TRIPTODUR.
- Some people taking triptorelin, the active ingredient in TRIPTODUR, have had serious allergic reactions. **Call your child's doctor or get emergency medical help right away if your child gets any of the following symptoms of a serious allergic reaction:**
  - skin rashes, redness, or swelling
  - severe itching
  - hives
  - trouble breathing or swallowing
  - fast heart beat
  - sweating

○ throat tightness, hoarseness ○ swelling of face, mouth, and tongue ○ dizziness or fainting

- pregnant or becomes pregnant. TRIPTODUR can cause birth defects or loss of the baby. If your child becomes pregnant call your doctor.

Before your child receives TRIPTODUR, tell your child's doctor about all of your child's medical conditions, including if they:

- have a history of mental (psychiatric) problems.
- have a history of seizures.
- have a history of epilepsy.
- have a history of brain or brain vessel (cerebrovascular) problems or tumors.
- are breastfeeding or plan to breastfeed. It is not known if TRIPTODUR passes into breastmilk.

Tell the doctor about all the medicines your child takes, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will your child receive TRIPTODUR?

- Your child's doctor should do tests to make sure your child has CPP before treating them with TRIPTODUR.
- TRIPTODUR must be given under the supervision of a doctor.
- TRIPTODUR is given as a single intramuscular (in the muscle) injection 1 time every 24 weeks.
- Keep all scheduled visits to the doctor. **Do not** delay a scheduled dose. The doctor will do regular exams and blood tests to check for signs of puberty.

What are the possible side effects of TRIPTODUR?

TRIPTODUR may cause serious side effects. See **"What is the most important information I should know about TRIPTODUR?"**

The most common side effects of TRIPTODUR include injection site reactions, menstrual (vaginal) bleeding, hot flush, headache, cough, and infections (bronchitis, gastroenteritis, influenza, nasopharyngitis, otitis externa, pharyngitis, sinusitis, and upper respiratory tract infection).

These are not all the possible side effects of TRIPTODUR. **Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.**

What are the ingredients in TRIPTODUR?

Active ingredient: triptorelin

Inactive ingredients: poly-*d,l*-lactide-co-glycolide, mannitol, carboxymethylcellulose sodium, and polysorbate 80

Distributed by: Arbor Pharmaceuticals, LLC, Atlanta, GA 30328
Manufactured by: Debiopharm Research & Manufacturing SA, CH-1920 Martigny, Switzerland

For more information about TRIPTODUR, please contact Arbor Pharmaceuticals, LLC at 1-866-516-4950.

This Medication Guide has been approved by the U.S. Food and Drug Administration Rev: 04/2022

arbor PHARMACEUTICALS, LLC

TRIP-MG-05