

ZOMACTON™

[somatropin (rDNA origin)] for Injection
5 mg and 10 mg

DESCRIPTION

ZOMACTON™ [somatropin (rDNA origin)] for Injection, a polypeptide of recombinant DNA origin, has 191 amino acid residues and a molecular weight of about 22,124 daltons. It has an amino acid sequence identical to that of human growth hormone of pituitary origin. ZOMACTON is a strain of *Escherichia coli* modified by insertion of the human growth hormone gene.

ZOMACTON is a sterile, white, lyophilized powder, intended for subcutaneous administration, after reconstitution with the accompanying diluent.

ZOMACTON 5 mg vial contains recombinant somatropin 5 mg and mannitol 30 mg. The 5 mg vial is supplied in a combination package with an accompanying 5 mL vial of diluting solution. The diluent contains bacteriostatic 0.9% sodium chloride injection, USP, (normal saline), 0.9% benzyl alcohol as a preservative, and water for injection.

ZOMACTON 10 mg vial contains recombinant somatropin 10 mg, mannitol 10 mg, disodium phosphate dodecahydrate 3.57 mg, and sodium dihydrogen phosphate dehydrate 0.79 mg. The 10 mg vial is supplied in a combination package with an accompanying 1 mL syringe of diluting solution. The diluent contains bacteriostatic water for injection with 0.33% metacresol as a preservative.

ZOMACTON is a highly-purified preparation. Reconstituted solutions have a pH in the range of 7.0 to 9.0.

CLINICAL PHARMACOLOGY

Clinical trials have demonstrated that ZOMACTON is equivalent in its therapeutic effectiveness and in its pharmacokinetic profile to those of human growth hormone of pituitary origin (somatropin). ZOMACTON stimulates linear growth in children who lack adequate levels of endogenous growth hormone. Treatment of growth hormone-deficient children with ZOMACTON produces increased growth rates and IGF-1 (Insulin-Like Growth Factor-1) concentrations that are similar to those seen after therapy with human growth hormone of pituitary origin.

Both ZOMACTON and somatropin have also been shown to have other actions including:

A. Tissue Growth

1. Skeletal Growth. ZOMACTON stimulates skeletal growth in patients with growth hormone deficiency. The measurable increase in body length after administration of ZOMACTON results from its effect on the epiphyseal growth plates of long bones. Concentration of IGF-1, which may play a role in skeletal growth, are low in the serum of growth hormone-deficient children but increase during treatment with ZOMACTON. Mean serum alkaline phosphatase concentrations are increased.
2. Cell Growth. It has been shown that there are fewer skeletal muscle cells in short statured children who lack endogenous growth hormone as

compared with normal children. Treatment with somatropin results in an increase in both the number and size of muscle cells.

3. Organ Growth. Somatropin influences the size of internal organs and it also increases red cell mass.

B. Protein Metabolism

Linear growth is facilitated, in part, by increased cellular protein synthesis. Nitrogen retention, as demonstrated by decreased urinary nitrogen excretion and serum urea nitrogen, results from treatment with somatropin.

C. Carbohydrate Metabolism

Children with hypopituitarism sometimes experience fasting hypoglycemia that is improved by treatment with somatropin. Large doses of somatropin may impair glucose tolerance.

D. Lipid Metabolism

Administration of somatropin to growth hormone-deficient patients mobilizes lipid, reduces body fat stores, and increases plasma fatty acids.

E. Mineral Metabolism

Sodium, potassium, and phosphorous are conserved by somatropin. Serum concentrations of inorganic phosphates increased in patients with growth hormone deficiency after therapy with ZOMACTON or somatropin. Serum calcium concentrations are not significantly altered in patients treated with either somatropin or ZOMACTON.

F. Connective Tissue Metabolism

Somatropin stimulates the synthesis of chondroitin sulfate and collagen as well as the urinary excretion of hydroxyproline.

PHARMACOKINETICS

Following intravenous administration of 0.1 mg/kg of ZOMACTON, the elimination half-life was about 0.42 hours (approximately 25 minutes) and the mean plasma clearance (\pm SD) was 133 (\pm 16) mL/min in healthy male volunteers.

In the same volunteers, after a subcutaneous injection of 0.1 mg/kg ZOMACTON to the forearm, the mean peak serum concentration (\pm SD) was 80 (\pm 50) ng/mL which occurred approximately 7 hours post-injection and the apparent elimination half-life was approximately 2.7 hours. Compared to intravenous administration, the extent of systemic availability from subcutaneous administration was approximately 70%.

INDICATION AND USAGE

ZOMACTON is indicated for the treatment of children who have growth failure due to an inadequate secretion of normal endogenous growth hormone.

CONTRAINDICATIONS

ZOMACTON is contraindicated in patients with a known hypersensitivity to somatropin or any of its excipients. Systemic hypersensitivity reactions have been reported with postmarketing use of somatropin products [see **WARNINGS**].

ZOMACTON 5 mg reconstituted with bacteriostatic 0.9% sodium chloride injection, USP (normal saline) (benzyl alcohol preserved) should not be administered to patients with a known sensitivity to benzyl alcohol [see **WARNINGS**].

ZOMACTON 10 mg reconstituted with bacteriostatic water for injection containing 0.33% metacresol should not be used if the patient is allergic to metacresol.

Somatropin should not be used for growth promotion in pediatric patients with closed epiphyses.

Somatropin is contraindicated in patients with active proliferative or severe non-proliferative diabetic retinopathy.

In general, somatropin is contraindicated in the presence of active malignancy. Any preexisting malignancy should be inactive and its treatment complete prior to instituting therapy with somatropin. Somatropin should be discontinued if there is evidence of recurrent activity. Since growth hormone deficiency may be an early sign of the presence of a pituitary tumor (or, rarely, other brain tumors), the presence of such tumors should be ruled out prior to initiation of treatment. Somatropin should not be used in patients with any evidence of progression or recurrence of an underlying intracranial tumor [see **WARNINGS**].

Treatment with pharmacologic amounts of somatropin is contraindicated in patients with acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure [see **WARNINGS**].

Somatropin is contraindicated in patients with Prader-Willi syndrome who are severely obese or have severe respiratory impairment [see **WARNINGS**]. ZOMACTON is not indicated for the treatment of pediatric patients who have growth failure due to genetically confirmed Prader-Willi syndrome.

WARNINGS

Increased mortality in patients with acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure has been reported after treatment with pharmacologic doses of somatropin [see **CONTRAINDICATIONS**]. Two placebo-controlled clinical trials in non-growth hormone deficient adult patients (n=522) with these conditions in intensive care units revealed a significant increase in mortality (42% vs. 19%) among somatropin-treated patients (doses 5.3 to 8 mg/day) compared to those receiving placebo. The safety of continuing somatropin treatment in patients receiving replacement doses for approved indications who concurrently develop these illnesses has not been established. Therefore, the potential benefit of treatment continuation with somatropin in patients experiencing acute critical illnesses should be weighed against the potential risk.

There have been reports of fatalities after initiating therapy with somatropin in pediatric patients with Prader-Willi syndrome who had one or more of the following risk factors: severe obesity, history of upper airway obstructions or sleep apnea, or unidentified respiratory infection. Male patients with one or more of these factors may be at greater risk than females. Patients with Prader-Willi syndrome should be evaluated for signs of upper airway obstruction and sleep apnea before initiation of treatment with somatropin. If during treatment with somatropin, patients show signs of upper airway obstruction (including onset of or increased snoring) and/or new onset sleep apnea, treatment should be interrupted. All patients with Prader-Willi syndrome treated with somatropin should also have effective weight control and be monitored for signs of respiratory infection, which should be diagnosed as early as possible and treated aggressively [see **CONTRAINDICATIONS**]. ZOMACTON is not indicated for the treatment of pediatric patients who have growth failure due to genetically confirmed Prader-Willi syndrome.

Serious systemic hypersensitivity reactions including anaphylactic reactions and angioedema have been reported with postmarketing use of somatropin products. Patients and caregivers should be informed that such reactions are possible and that prompt medical attention should be sought if an allergic reaction occurs [see **CONTRAINDICATIONS**].

Cases of pancreatitis have been reported rarely in children and adults receiving somatropin treatment, with some evidence supporting a greater risk in children compared with adults. Published literature indicates that girls who have Turner syndrome may be at greater risk than other somatropin-treated children. Pancreatitis should be considered in any somatropin-treated patient, especially a child, who develops persistent, severe abdominal pain.

Benzyl alcohol, a component used to reconstitute the ZOMACTON 5 mg vial, has been associated with serious adverse events and death, particularly in pediatric patients. The “gaspings syndrome,” (characterized by central nervous system depression, metabolic acidosis, gasping respirations, and high levels of benzyl alcohol and its metabolites found in the blood and urine) has been associated with benzyl alcohol dosages >99 mg/kg/day in neonates and low-birth weight neonates. Additional symptoms may include gradual neurological deterioration, seizures, intracranial hemorrhage, hematologic abnormalities, skin breakdown, hepatic and renal failure, hypotension, bradycardia, and cardiovascular collapse. Practitioners administering this and other medications containing benzyl alcohol should consider the combined daily metabolic load of benzyl alcohol from all sources.

When administering ZOMACTON 5 mg to newborns, reconstitute with sterile normal saline for injection, USP. **WHEN RECONSTITUTING WITH STERILE NORMAL SALINE, USE ONLY ONE DOSE PER VIAL AND DISCARD THE UNUSED PORTION.**

PRECAUTIONS

General

ZOMACTON therapy should be carried out under the regular guidance of a physician who is experienced in the diagnosis and management of pediatric patients with growth hormone deficiency.

In childhood cancer survivors who were treated with radiation to the brain/head for their first neoplasm and who developed subsequent GHD and were treated with somatropin, an increased risk of a second neoplasm has been reported. Intracranial tumors, in particular meningiomas, were the most common of these second neoplasms. In adults, it is unknown whether there is any relationship between somatropin replacement therapy and CNS tumor recurrence [see **CONTRAINDICATIONS**]. Monitor all patients with a history of GHD secondary to an intracranial neoplasm routinely while on somatropin therapy for progression or recurrence of the tumor.

Because children with certain rare genetic causes of short stature have an increased risk of developing malignancies, practitioners should thoroughly consider the risks and benefits of starting somatropin in these patients. If treatment with somatropin is initiated, these patients should be carefully monitored for development of neoplasms.

Monitor patients on somatropin therapy carefully for increased growth, or potential malignant changes, of preexisting nevi.

Treatment with somatropin may decrease insulin sensitivity, particularly at higher doses in susceptible patients. As a result, previously undiagnosed impaired glucose tolerance and overt diabetes mellitus may be unmasked during somatropin treatment. New-onset type 2 diabetes mellitus has been reported in patients. Therefore, glucose levels should be monitored periodically in all patients treated with somatropin, especially in those with risk factors for diabetes mellitus, such as obesity, Turner syndrome, or a family history of diabetes mellitus. Patients with preexisting type 1 or type 2 diabetes mellitus or impaired glucose tolerance should be monitored closely during somatropin therapy. The doses of antihyperglycemic drugs (i.e., insulin or oral agents) may require adjustment when somatropin therapy is instituted in these patients.

Patients receiving somatropin therapy who have or are at risk for pituitary hormone deficiency(s) may be at risk for reduced serum cortisol levels and/or unmasking of central (secondary) hypoadrenalism. In addition, patients treated with glucocorticoid replacement for previously diagnosed hypoadrenalism may require an increase in their maintenance or stress doses following initiation of somatropin treatment [see **DRUG INTERACTIONS**].

Undiagnosed/untreated hypothyroidism may prevent an optimal response to somatropin, in particular, the growth response in children. Patients with Turner syndrome have an inherently increased risk of developing autoimmune thyroid disease and primary hypothyroidism. In patients with growth hormone deficiency, central (secondary) hypothyroidism may first become evident or worsen during somatropin treatment. Therefore, patients treated with somatropin should have periodic thyroid function tests and thyroid hormone replacement therapy should be initiated or appropriately adjusted when indicated.

Patients with endocrine disorders, including growth hormone deficiency, may have an increased incidence of slipped capital femoral epiphysis. Any child who develops a limp or complains of hip or knee pain during somatropin therapy should be evaluated.

Intracranial hypertension (IH) with papilledema, visual changes, headache, nausea and/or vomiting has been reported in a small number of patients treated with growth hormone

products. IH has been reported more frequently after treatment with IGF-1. Symptoms usually occur within the first eight weeks after the initiation of growth hormone therapy. In all reported cases, IH-associated signs and symptoms resolved rapidly after temporary suspension or termination of therapy. Fundoscopic examination should be performed routinely before initiating treatment with somatropin to exclude preexisting papilledema and periodically during the course of somatropin therapy. If papilledema is observed by fundoscopy during somatropin treatment, treatment should be stopped. If somatropin induced idiopathic IH is diagnosed, treatment with somatropin can be restarted at a lower dose after IH-associated signs and symptoms have resolved.

Progression of scoliosis can occur in children who experience rapid growth. Because somatropin increases growth rate, patients with a history of scoliosis who are treated with somatropin should be monitored for progression of scoliosis.

Bone age should be monitored periodically during somatropin administration, especially in patients who are pubertal and/or receiving concomitant thyroid hormone replacement therapy. Under these circumstances, epiphyseal maturation may progress rapidly.

When somatropin is administered subcutaneously at the same site over a long period of time, tissue atrophy may result. This can be avoided by rotating the injection site.

Information for Patients

Patients being treated with ZOMACTON and/or their caregivers should be informed about the potential benefits and risks associated with treatment. See the patient information included with the product and/or injection device. This information is intended to aid in the safe and effective administration of the medication. It is not a disclosure of all possible adverse or intended effects.

Patients and caregivers who will administer ZOMACTON should receive appropriate training and instruction on the proper use of ZOMACTON from the physician or other suitable qualified health care professional. A puncture-resistant container for the disposal of used needles and syringes should be strongly recommended. Patients and/or caregivers should be thoroughly instructed in the importance of proper disposal, and cautioned against any reuse of needles and syringes.

Laboratory Tests

Serum levels of inorganic phosphorus, alkaline phosphatase, and IGF-1 may increase after somatropin therapy.

Drug Interactions

The microsomal enzyme 11 β -hydroxysteroid dehydrogenase type 1 (11 β HSD-1) is required for conversion of cortisone to its active metabolite, cortisol, in hepatic and adipose tissue. Growth hormone and somatropin inhibit 11 β HSD-1. Consequently, individuals with untreated GH deficiency have relative increases in 11 β HSD-1 and serum cortisol. Introduction of somatropin treatment may result in inhibition of 11 β HSD-1 and reduced serum cortisol concentrations. As a consequence, previously undiagnosed central (secondary) hypoadrenalism may be unmasked and glucocorticoid replacement may be required in patients treated with somatropin. In addition, patients treated with glucocorticoid replacement for previously diagnosed hypoadrenalism may require an increase in their maintenance or stress doses following initiation of somatropin treatment; this may be especially true for patients treated with cortisone acetate and prednisone since conversion of these drugs to their biologically active metabolites is dependent on the activity of 11 β HSD-1 [see **PRECAUTIONS**].

Pharmacologic glucocorticoid therapy and supraphysiologic glucocorticoid treatment may attenuate the growth promoting effects of somatropin in children. Therefore, glucocorticoid replacement dosing should be carefully adjusted in children receiving concomitant somatropin and glucocorticoid treatments to avoid both hypoadrenalism and an inhibitory effect on growth.

Limited published data indicate that somatropin treatment increases cytochrome P450 (CP450) mediated antipyrine clearance in man. These data suggest that somatropin administration may alter the clearance of compounds known to be metabolized by CP450 liver enzymes (e.g., corticosteroids, sex steroids, anticonvulsants, cyclosporine). Careful monitoring is advisable when somatropin is administered in combination with other drugs known to be metabolized by CP450 liver enzymes.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis, mutagenesis and reproduction studies have not been conducted with ZOMACTON.

Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted with ZOMACTON. It is also not known whether ZOMACTON can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. ZOMACTON should be given to a pregnant woman only if clearly needed.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ZOMACTON is administered to a nursing woman.

Geriatric Use

The safety and effectiveness of somatropin in patients aged 65 and over has not been evaluated in clinical studies. Elderly patients may be more sensitive to the action of somatropin, and may be more prone to develop adverse reactions.

ADVERSE REACTIONS

The following adverse reactions have been observed during appropriate use of somatropin: headaches (children and adults), gynecomastia (children) and pancreatitis (children and adults) [see **WARNINGS**].

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to ZOMACTON with the incidence of antibodies to other products may be misleading. With respect to growth hormone, antibody binding capacities below 2 mg/L have not been associated with growth attenuation. In some cases, when binding capacity exceeds 2 mg/L, growth attenuation has been observed.

None of the patients with anti-GH antibodies in the clinical studies experienced decreased linear growth response to ZOMACTON or any other associated adverse event. Injection site reactions (e.g., pain, bruise) occurred in 8 of the 164 treated patients.

Leukemia has been reported in a small number of patients treated with other growth hormone products. It is uncertain whether this risk is related to the pathology of growth hormone deficiency itself, growth hormone therapy, or other associated treatments such as radiation therapy for intracranial tumors.

Serious systemic hypersensitivity reactions including anaphylactic reactions and angioedema have been reported with postmarketing use of somatropin products [see **WARNINGS**].

New-onset type 2 diabetes mellitus has been reported.

OVERDOSAGE

The recommended dosage of up to 0.1 mg/kg of body weight 3 times per week (up to 0.3 mg/kg/week) should not be exceeded. Acute overdose could cause initial hypoglycemia and subsequent hyperglycemia. Repeated use of doses in excess of those recommended could result in signs and symptoms of gigantism and/or acromegaly consistent with the known effects of excess human growth hormone.

DOSAGE AND ADMINISTRATION

The recommended dose is up to 0.1 mg/kg administered subcutaneously three (3) times per week (up to 0.3 mg/kg/week).

ZOMACTON 5 mg should be reconstituted with 1-5 mL of bacteriostatic 0.9% sodium chloride for injection, USP (benzyl alcohol preserved). Reconstituted ZOMACTON 5 mg vials should not be used if the patient has a known sensitivity to benzyl alcohol. Benzyl alcohol as a preservative in bacteriostatic normal saline, USP, has been associated with toxicity in newborns. **WHEN ADMINISTERING ZOMACTON TO NEWBORNS, RECONSTITUTE WITH STERILE NORMAL SALINE FOR INJECTION, USP.**

ZOMACTON 10 mg should be reconstituted with 1 mL syringe of bacteriostatic water for injection containing 0.33% metacresol as a preservative. Reconstituted ZOMACTON 10 mg vials should not be used if the patient is allergic to metacresol.

The stream of normal saline should be aimed against the side of the vial to prevent foaming. Swirl the vial with a GENTLE rotary motion until the contents are completely dissolved and the solution is clear. DO NOT SHAKE. Since ZOMACTON is a protein, shaking or vigorous mixing will cause the solution to be cloudy. If the resulting solution is cloudy or contains particulate matter, the contents MUST NOT be injected.

Occasionally, after refrigeration, some cloudiness may occur. This is not unusual for proteins like ZOMACTON. Allow the product to warm to room temperature. If cloudiness persists or particulate matter is noted, the contents MUST NOT be used.

Before and after injection, the septum of the vial should be wiped with rubbing alcohol or an alcoholic antiseptic solution to prevent contamination of the contents by repeated needle insertions.

ZOMACTON 5 mg and 10 mg can be administered using a standard sterile disposable syringe or a ZOMA-Jet™ Needle-Free injection device. For proper use, please refer to the **User's Manual** provided with the administration device.

STABILITY AND STORAGE

Before Reconstitution

Vials of ZOMACTON (5 and 10 mg) are stable when refrigerated at 36° to 46°F (2° to 8°C). Avoid freezing the accompanying diluent. Expiration dates are stated on the labels.

After Reconstitution

ZOMACTON 5 mg is stable for up to 14 days when reconstituted with bacteriostatic 0.9% sodium chloride (normal saline), USP, and stored in a refrigerator at 36° to 46°F (2° to 8°C). Do not freeze the reconstituted solution.

ZOMACTON 10 mg is stable for up to 28 days when reconstituted with 1 mL syringe of bacteriostatic water for injection containing 0.33% metacresol as a preservative, and stored in a refrigerator at 36° to 46°F (2° to 8°C). Do not freeze the reconstituted solution.

HOW SUPPLIED

ZOMACTON [somatropin (rDNA origin)] for injection is supplied as 5 mg and 10 mg of lyophilized, sterile somatropin per vial.

ZOMACTON 5 mg carton (NDC 55566-1801-1) contains one vial of ZOMACTON (5 mg per vial) and one vial of diluent [5 mL of bacteriostatic 0.9% sodium chloride for injection, USP (benzyl alcohol preserved)], and is supplied in single cartons.

ZOMACTON 10 mg carton (NDC 55566-1901-1) contains one vial of ZOMACTON (10 mg per vial), one syringe of diluent [1 mL of bacteriostatic water for injection with 0.33% metacresol as preservative] and a 25G reconstitution needle, and is supplied in single cartons.

ZOMACTON 10 mg carton (NDC 55566-1902-1) contains one vial of ZOMACTON

(10mg per vial), one syringe of diluent [1 mL of bacteriostatic water for injection with 0.33% metacresol as preservative], 1 vial adapter, and is supplied in single cartons.

Rx only.

Manufactured for:
Ferring Pharmaceuticals Inc., Parsippany,
NJ 07054

Manufactured in Germany

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Rev. 12/2016

ZOMACTON™
(zoh-MACK-ton)
[somatropin (rDNA origin)]
for Injection

Read the Instructions for Use that come with your ZOMACTON before you start using it and each time you get a refill. There may be new information. This leaflet does not take the place of talking to your healthcare provider about your medical condition or treatment. Before you use ZOMACTON for the first time, make sure your healthcare provider shows you the right way to use it.

Supplies needed for your ZOMACTON Injection

- **ZOMACTON 5mg (See Figure A)** containing:
 - 1 vial of ZOMACTON 5mg growth hormone in a powder
 - 1 vial of liquid (diluent) containing Bacteriostatic 0.9% Sodium Chloride Injection, USP (5mL). This is used to mix your ZOMACTON 5mg.

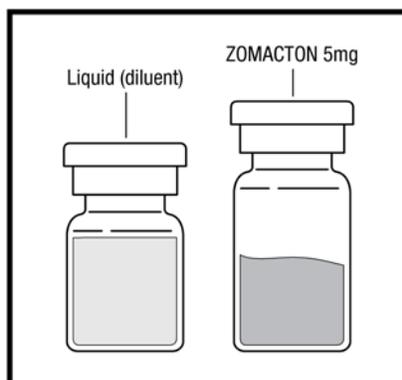


Figure A

or

- **ZOMACTON 10mg (See Figure B)** containing:
 - 1 vial of ZOMACTON 10mg growth hormone in a powder
 - 1 syringe of liquid (diluent) containing Bacteriostatic Water for Injection with 0.33% Metacresol as a preservative (1mL). This is used to mix your ZOMACTON 10mg.
 - 25 gauge mixing needle

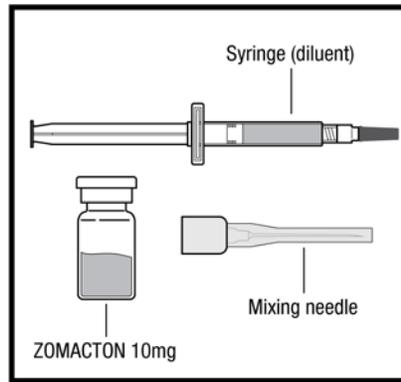


Figure B

The following additional supplies (**See Figure C**) will be needed:

- Syringe and needle for injection. Your healthcare provider will tell you the size of the syringe and needle to use.
- Alcohol swab
- Puncture-resistant container (**See Step 4: Disposing of used syringes, needles, and vials**)

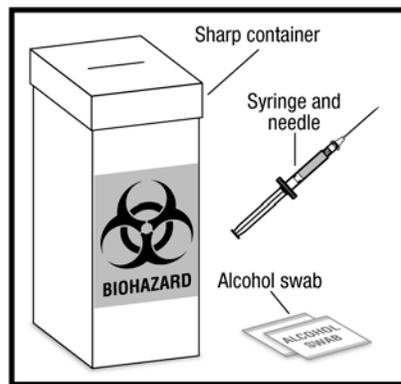


Figure C

Preparing for Your ZOMACTON Injection

- Place the supplies you will need on a clean, flat surface in a well-lit area.
- Wash your hands thoroughly with soap and water.

Important: The liquids are different for the 5mg and 10mg vials.

- **Do not** use the 5mg liquid with the 10mg ZOMACTON.
- **Do not** use the 10mg liquid with the 5mg ZOMACTON.

Preparing ZOMACTON 5mg Liquid for Injection:

- Remove the hard plastic cap from the top of the liquid vial by gently pushing up on the edge of the cap (**See Figure D**). **Do not** remove the rubber stopper.

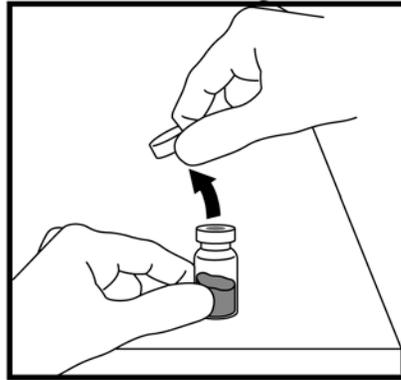


Figure D

- Use an alcohol swab to wipe off the top of the liquid vial (**See Figure E**). After cleaning, **do not** touch the rubber stopper.

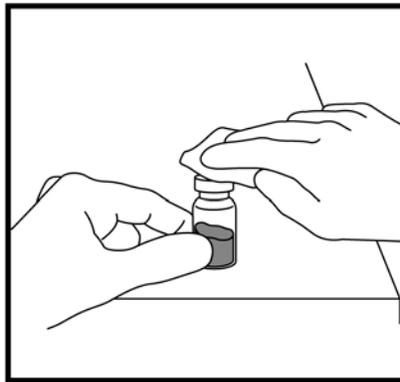


Figure E

- Remove the needle cap from the syringe while making sure you **do not** touch the needle (**See Figure F**). **Do not** throw away the needle cap.

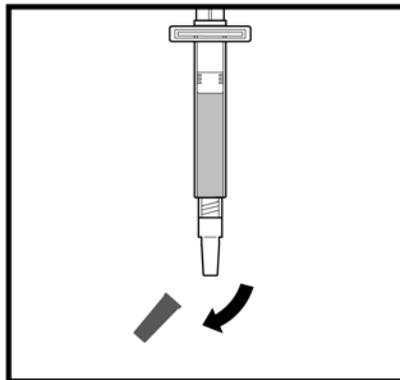


Figure F

- Hold the barrel of the syringe with **1** hand and pull back on the plunger with the other hand until you have drawn up the amount of air that is the same as the amount of liquid your healthcare provider has prescribed (**See Figure G**).

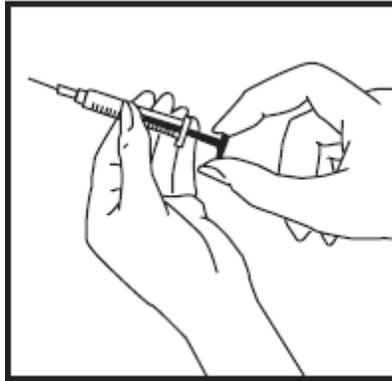


Figure G

- Insert the needle into the liquid vial through the center of the clean rubber stopper. Push down on the plunger until all the air is released into the vial (**See Figure H**).

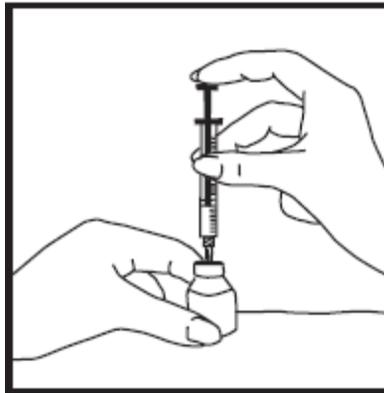


Figure H

- Hold the vial with **1** hand and carefully turn the vial upside down making sure the syringe needle stays in the vial. **The tip of the needle should be below the surface of the liquid.**
- With your other hand, gently pull back the plunger until the amount of liquid your healthcare provider prescribed is in the syringe (**See Figure I**).



Figure I

When the syringe is correctly filled with the liquid, remove the syringe and needle from the vial and recap the needle.

Preparing ZOMACTON 10mg Liquid for Injection:

- Remove the syringe tip cap from the top of the pre-filled liquid syringe and attach the **25G** mixing needle that comes with your ZOMACTON (See **Figure J**).

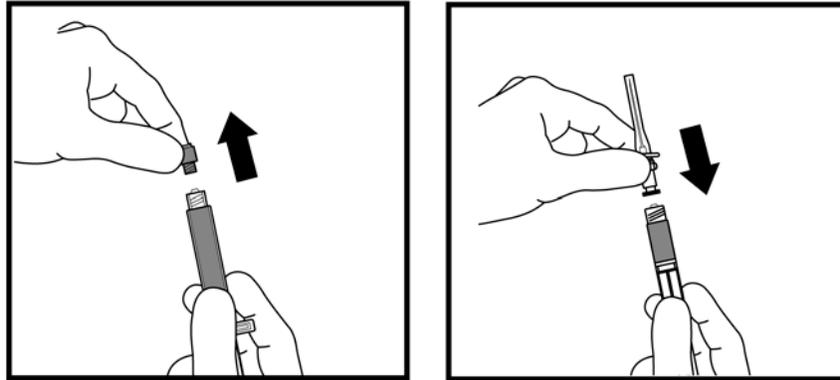


Figure J

Diluting Your ZOMACTON

- **Only** use the liquid that comes with the 5mg ZOMACTON to mix the 5mg growth hormone. **Only** use the liquid that comes with the 10mg ZOMACTON to mix the 10mg growth hormone.
- Remove the hard plastic cap of the growth hormone vial (See **Figure K**).

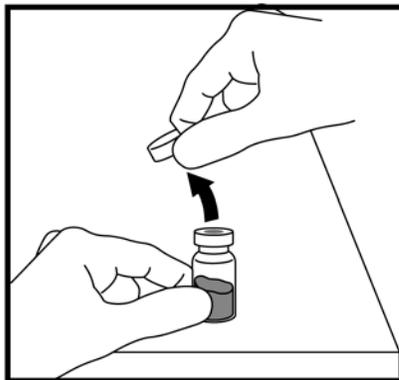


Figure K

- Clean the top of the growth hormone vial with an alcohol swab (See **Figure L**).

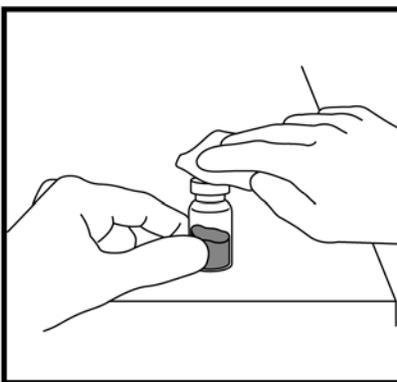


Figure L

- Remove the needle cap from the syringe filled with liquid and insert the needle into the center of the rubber stopper on the growth hormone vial (See Figure M).

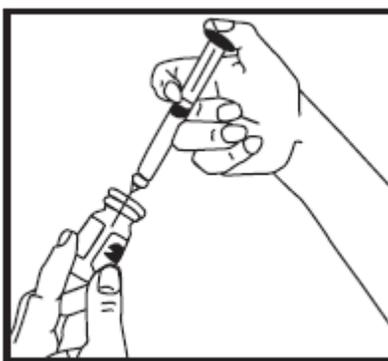


Figure M

- Point the needle toward the side of the vial and slowly push the plunger so that the liquid squirts onto the side of the vial and **not** directly onto the powder.
- When all the liquid is in the growth hormone vial, remove the needle from the vial (See Figure N).

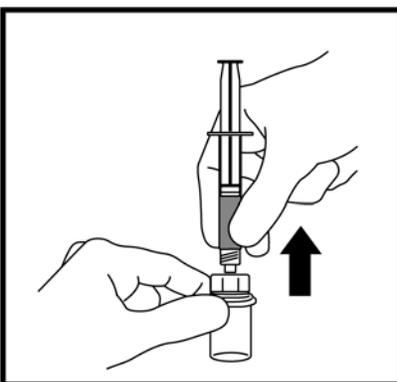


Figure N

- Recap the needle and throw away the syringe.

Mixing ZOMACTON

- Hold the vial between your hands and gently roll it until the mixture is clear. **Do not shake the vial.** Your ZOMACTON is ready for injection.
- Sometimes the vial may need to sit a few seconds before the mixture becomes clear. **Do not** use the mixture in the vial if it remains cloudy or you see particles floating in the mixture. If air bubbles appear, let the growth hormone sit for a while until they disappear.
- Write the date you mixed the growth hormone on the vial label. The **5 mg** vial must be used within **14** days. The 10mg vial must be used within **28** days.
- Store your **mixed** growth hormone and all **unopened vials** of growth hormone in the refrigerator at 36°F to 46°F (2°C to 8°C). **Do not** freeze.

Step 1: Preparing the Injection

You are now ready for your ZOMACTON injection.

- Wash your hands thoroughly with soap and water.
- Check that the vial of growth hormone you are using is clear and that the date of mixing is within **14** days if you are using ZOMACTON **5mg** or **28** days if you are using ZOMACTON **10mg**.
- Clean the top of the growth hormone vial with an alcohol swab. **Do not** touch the rubber stopper after cleaning (**See Figure O**).

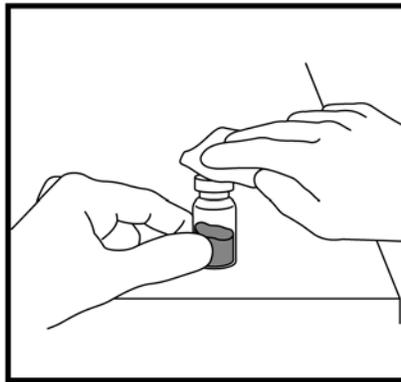


Figure O

- Remove the needle cap from the syringe and insert the needle into the center of the rubber stopper on the growth hormone vial (**See Figure P**).

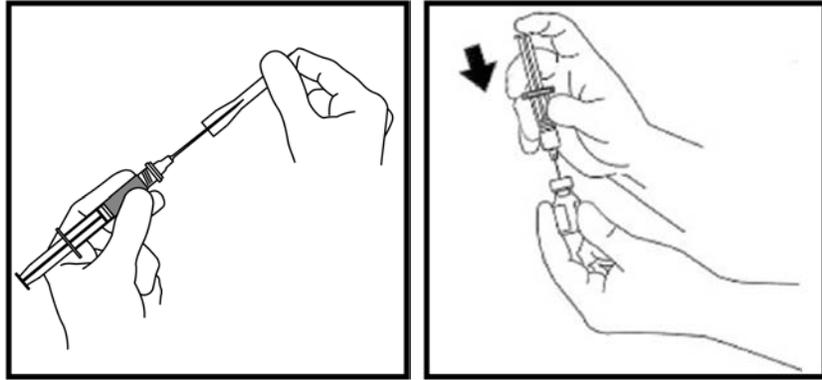


Figure P

- Gently pull back the plunger until the amount of growth hormone solution your healthcare provider has prescribed is in the syringe (**See Figure Q**).

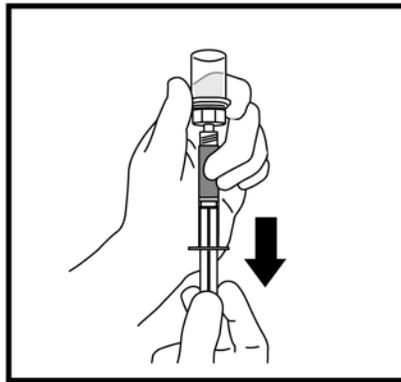


Figure Q

- Remove the needle from the vial when the syringe is correctly filled with the solution (**See Figure R**). Recap the needle.

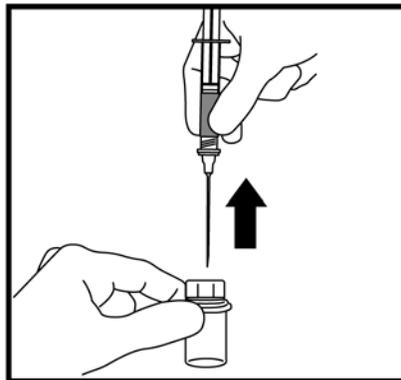


Figure R

Step 2: Choosing an Injection Site

- There are different sites you can use for your injections. These sites should be rotated (**See Figure S**).

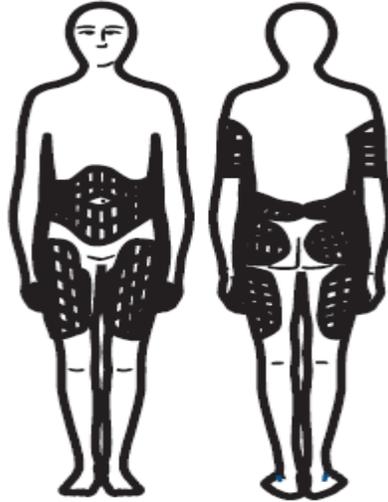


Figure S

If you notice any of the following signs, contact your healthcare provider:

- A lump, bruise or redness at the injection site that does not go away.
- Any sign of infection at the injection site (pus, redness, heat or persistent pain).
- Severe, sharp pain or ache at injection site that does not go away.
- Rash at the injection site.

Step 3: Injecting ZOMACTON

Using a circular motion, clean the injection site with an alcohol swab, starting at the injection site and moving outward about 2 inches. Let the skin air dry.

- Check that the correct dose is in the syringe.
- Remove the needle cap. Hold the syringe like a pencil in 1 hand.
- With your free hand, pinch the skin around the site with the thumb and forefinger of the other hand (**See Figure T**). Quickly insert the needle into the skin at a 45° - 90° angle with a quick, dart-like motion.

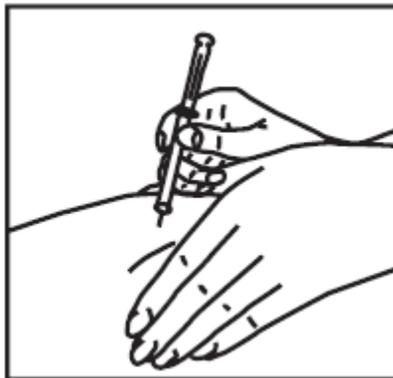


Figure T

- Holding the syringe in place, pull back a little on the plunger and check to see if any blood flows into the syringe (**See Figure U**). If you **see blood in the syringe** it means that you have entered a blood vessel. **Do not** inject ZOMACTON. Withdraw the needle. Throw away the syringe and needle in a puncture-resistant container. Do not use the same syringe or any of the other supplies that you used for this injection. Repeat the steps to prepare a new syringe for injection. Choose and clean a new injection site.

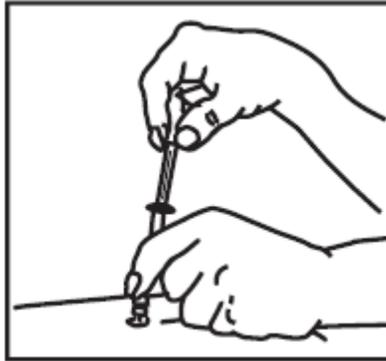


Figure U

- If no blood appears in the syringe, slowly push down plunger all the way until the syringe is completely empty (**See Figure V**).

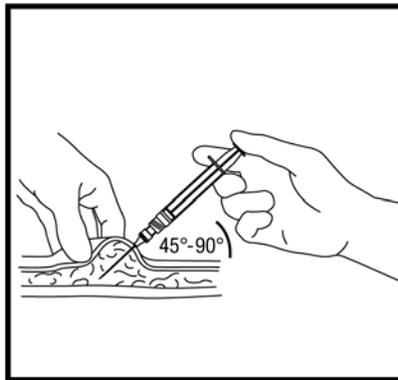


Figure V

- Quickly remove the needle from the skin and apply pressure to the injection site with a dry sterile gauze pad or cotton ball. A drop of blood may appear. Apply a small bandage if needed. Throw away the needle and syringe in your puncture-resistant disposal container.
- Do not share your syringes, needles, or vials with anyone else. You may give them or get an infection from them.

Step 4: Disposing of used syringes, needles, and vials

- To prevent needle-stick injury and spread of infection, do not try to re-cap the needle.
- Place used needles, syringes, and vials in a closeable, puncture-resistant container. You may use a sharps container (such as a red biohazard

container), hard plastic container (such as a detergent bottle), or metal container (such as an empty coffee can). Do not use glass or clear plastic containers. Ask your healthcare provider for instructions on the right way to throw away (dispose of) the container. There may be state and local laws about how you should throw away used needles and syringes.

- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
 - made of a heavy-duty plastic,
 - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
 - upright and stable during use,
 - leak-resistant, and
 - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: <http://www.fda.gov/safesharpsdisposal>
- **Do not throw used needles, syringes, or vials in your household trash or recycle.**
- Keep the disposal container, needles, syringes, and vials of ZOMACTON out of reach of children.

This Instructions for Use has been approved by the Food and Drug Administration.

Manufactured for:
Ferring Pharmaceuticals Inc., Parsippany, NJ 07054
Manufactured in Germany

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ZOMA-Jet™ 10

Instructions for Use



For use with
ZOMACTON™
[somatropin (rDNA origin)] for Injection
10 mg vial

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The ZOMA-Jet™ 10 is a device used to administer ZOMACTON™ human growth hormone of recombinant DNA (rDNA) origin.

Do not share the ZOMA-Jet™ 10 device, the needle-free head, or the ZOMACTON™ 10 mg vial with anyone else. You may give an infection to them or get an infection from them.

Parts of the ZOMA-Jet™ 10



Figure A

Supplies you will need to mix a ZOMACTON™ 10 mg Vial

- Prefilled Syringe (liquid)
- ZOMACTON™ 10 mg Vial (powder)
- Vial Adapter
- Alcohol Swab



Figure B

Mix a ZOMACTON™ 10 mg vial

ZOMACTON™ 10 mg is not ready to be used right away. You must mix (reconstitute) the dry powder in the ZOMACTON™ 10 mg vial with the Prefilled Syringe using the Vial Adapter. Both the Prefilled Syringe and Vial Adapter come with your medicine.

- Remove the plastic cap from the ZOMACTON™ 10 mg vial and clean the top of the vial with an alcohol swab. See Figure C.
- Open a new Vial Adapter package. The Vial Adapter is sterile as long as the package is not opened or damaged.
- Place the pointed tip of the Vial Adapter in the center of the vial. **Firmly** push down turning left, counterclockwise, gently until it pushes through the rubber seal and snaps onto the vial. See Figure D.



Figure C



Figure D

- Grasp the Vial Adapter just under the cap with 1 hand. Pull the cap up with your other hand to remove it. See Figure E. **Do not** hold the vial upside down. This may cause the vial to leak.



Figure E

- Remove the rubber cap from the Prefilled Syringe. See Figure F.



Figure F

- Insert the nipple end of the syringe into the Vial Adapter and **firmly** push down to secure it in place. See Figure G.



Figure G

- **Slowly** push the plunger into the syringe to inject all of the liquid into the ZOMACTON™ 10 mg vial. All of the liquid must be removed from the syringe to make sure you get the right dose.

Firmly hold the Vial Adapter with 1 hand and remove the emptied Syringe (along with the already connected Syringe Mating Piece) with your other hand. See Figure H.



Figure H

- Hold the vial between your hands and gently roll it to dissolve the mixture until it is clear. **Do not** shake the vial. **Do not** use mixed ZOMACTON™ if it is cloudy or if you see particles floating in the mixture. Call the ZoGo Patient support at 844.944.ZOGO (9646) if your ZOMACTON™ is cloudy.

Important: Write the date you mixed ZOMACTON™ on the vial label with a marker. Use your mixed ZOMACTON™ 10 mg vial within 28 days.

The ZOMACTON™ 10 mg vial is now mixed and ready for use with the ZOMA-Jet™ 10.

Reset the ZOMA-Jet™ 10

- Hold the ZOMA-Jet™ 10 device so that you can see the Dosage Window. Turn the Winding Grip in the direction of “Reset” until you see the black bar in the Dosage Window. See Figure I.

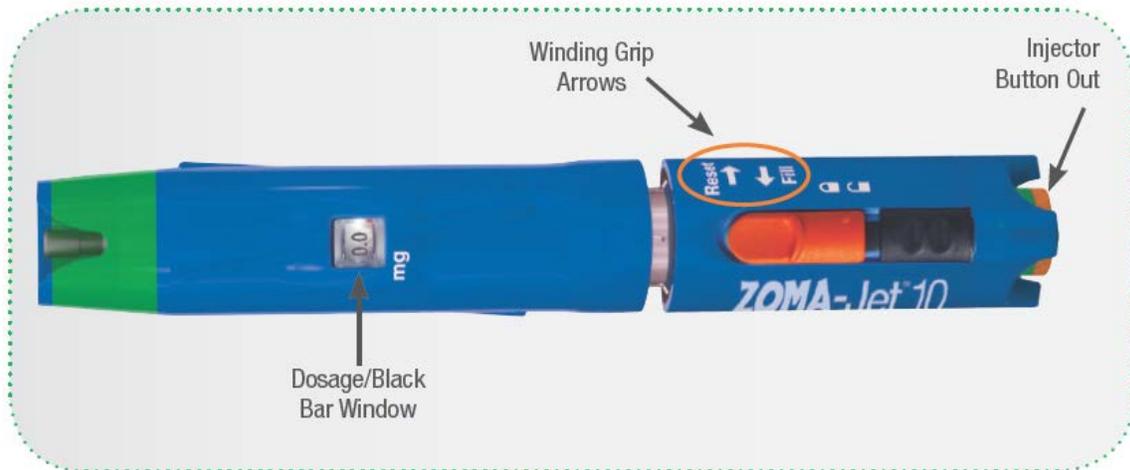


Figure I

Important: Do not turn the Winding Grip beyond the black bar. You should be able to see the green band on the Injector Button.

- Turn the Winding Grip in the direction of “Fill” until you see 0.0 in the Dosage Window.

The ZOMA-Jet™ 10 is now reset and ready for use.

Attach a Needle-Free Head

- Reset the device (see page 6).
- Open a new Needle-Free Head package. See Figure J. The Needle-Free Head is sterile as long as the package is not opened or damaged. **Do not** remove the cap while attaching the Needle-Free Head.

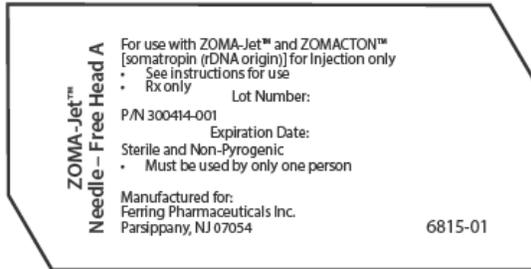


Figure J

Important: Your injection training nurse will let you know if Needle-Free Head size B or C is needed. If it is determined that you need size B or C, call the ZoGo Patient Support Program at 844.944.ZOGO (9646).

Write down the date of opening a new Needle-Free Head in your Daily Planner. **Important:** Each Needle-Free Head should be used for only 1 week.

- Line up the square blocks of the Needle-Free Head with the Viewing Notch of the ZOMA-Jet™ 10. See Figure K.
- **Firmly** push the Needle-Free Head straight into the Injector Body until it stops and **the ring can no longer be seen**.

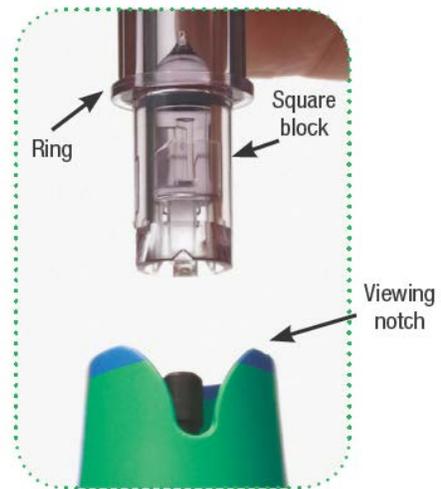


Figure K



Figure L

- **While pushing down** on the Needle-Free Head, turn right (clockwise) until it locks into place and you hear a click. The tabs on the side of the Needle-Free Head must line up with the marks on the ZOMA-Jet™ 10. Pull straight up on the Needle-Free Head to make sure it is locked into place. See Figure L.

Prime the ZOMA-Jet™ 10

You must prime your ZOMA-Jet™ 10 with ZOMACTON™ 10 mg each time you use a new Needle-Free Head and to make sure you get the right dose. Priming also removes most of the air bubbles inside the Needle-Free Head.

Important: Make sure that the Injector Button is popped out and that 0.0 is showing in the Dosage Window of the ZOMA-Jet™ 10 before you begin the following steps.



Figure M

- Turn the ZOMA-Jet™ 10 over so that the vial is upside down.
- Turn the Winding Grip in the direction of “Fill” until **0.1** appears in the Dosage Window. See Figure N.

- Remove the cap from the Needle-Free Head. Line up the tabs on the Needle-Free Head with the slots in the Vial Adapter and push straight down until it locks into place. See Figure M.



- Turn the ZOMA-Jet™ 10 back over so that the vial can be placed on a flat surface. Hold on to the Vial Adapter and pull the ZOMA-Jet™ 10 **straight off**. See Figure O.



Figure O

- Unlock the safety switch and point your ZOMA-Jet™ 10 so that it is facing down. See Figure P. Press the Injector Button to empty the liquid from the ZOMA-Jet™ 10. See Figure Q.



Figure P

Important: Do not point and press the Injector Button towards any person.



Figure Q

Your ZOMA-Jet™ 10 is now primed.

Inject with the ZOMA-Jet™ 10

You are now ready for your injection.

- Step 1.** Turn the Winding Grip in the direction of “Reset” until you see the black bar in the Dosage Window. You should be able to see the green band on the Injector Button. See Figure R.

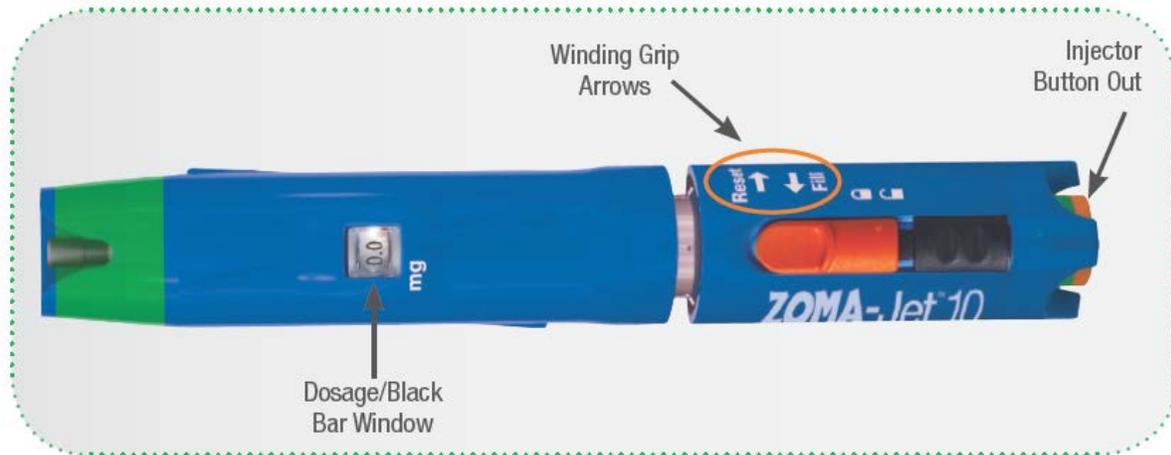


Figure R



Figure S

- Step 2.** Turn the Winding Grip in the direction of “Fill” until you see 0.0 in the Dosage Window.

- Step 3.** Line up the tabs on the Needle-Free Head with the slots in the Vial Adapter and push straight down until it locks into place. See Figure S.

Step 4. Turn the ZOMA-Jet™ 10 over so that the vial is upside down.

Step 5. Turn the Winding Grip in the direction of “Fill” until you see your prescribed dose in the Dosage Window. If you go beyond the dose your doctor prescribed, turn the Winding Grip in the opposite direction to your prescribed dose. See Figure T.

Important: If you see air bubbles inside of the Needle-Free Head, firmly tap the side of the ZOMA-Jet™ 10 with your finger to move them to the top. Turn the Winding Grip in the direction of “Reset” until the bubbles go into the vial. Fill the ZOMA-Jet™ 10 to your prescribed dose.



Figure U



Figure T

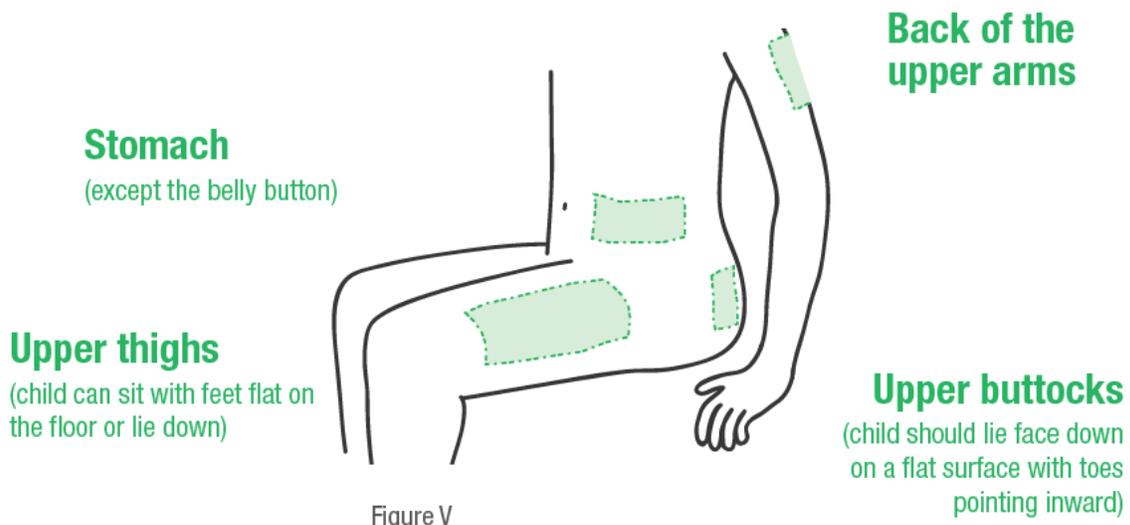
Important: Do not wind beyond the red bar in either direction.

Step 6. Turn the ZOMA-Jet™ 10 over so that the vial can be placed on a flat surface. Hold on to the Vial Adapter and pull the ZOMA-Jet™ 10 **straight off**. See Figure U.

Follow these instructions if you need another vial of ZOMACTON™ 10 mg to get your full dose:

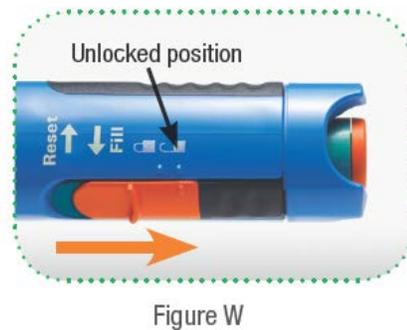
- Mix (reconstitute) a second ZOMACTON™ 10 mg vial (refer back to the “Mix a ZOMACTON™ 10 mg Vial” section on pages 3–5).
- Repeat steps 3–6 on pages 10–11

- Step 7.** Sit or lie down so that the injection site can be seen clearly and your muscles are relaxed.
- Step 8.** Choose an injection site with fatty tissue from the following places. See Figure V. Choose a different site each time you inject ZOMACTON™.



- Step 9.** Wipe the Needle-Free Head with an alcohol swab and unlock the Safety Switch. See Figure W. Now that the Needle-Free Head has been cleaned, be sure not to touch the tip before injecting. Clean the injection site with an alcohol swab.

Important: Each Needle-Free Head should be used for only 1 week.



- Step 10.** Place the ZOMA-Jet™ 10 firmly against the skin (**do not** pinch) at a **right angle** to the injection site, then press the Injector Button. See Figure X. Hold in place for 2 seconds after you hear a noise. This means that the injection is complete.

You have now injected with the ZOMA-Jet™ 10.

Evaluate your Injections

The following may happen at the injection site:

- Small amount of dampness
- Pinpoint of blood
- A tingly sensation

Important: If you feel pain, discomfort, or ZOMACTON™ leaks from the injection site, or you have problems with injecting, call ZoGo Patient Support at 844.944.ZOGO (9646).

If you experience an adverse event, please discuss it with your doctor. You are encouraged to report adverse events of prescription drugs to Ferring Pharmaceuticals at 1-888-FERRING (1-888-337-7464). You can also call FDA at 1-800-FDA-1088 or visit the FDA website www.fda.gov/medwatch.

Store the ZOMA-Jet™ 10 and ZOMACTON™ 10 mg Vial

Step 11. After the injection is complete, turn the Winding Grip in the direction of “Reset” until you see the black bar in the Dosage Window. You should be able to see the green band on the Injector Button.

Step 12. Turn the Winding Grip in the direction of “Fill” until you see 0.0 in the Dosage Window. This will reset the device. See Figure Y.



Figure Y

Important: The ZOMA-Jet™ 10 must be stored with the green band of the injector button visible **and** 0.0 in the Dosage Window or the Needle-Free Head will break.

Step 13. Wipe the Needle-Free Head with an alcohol swab. Make sure the Safety Switch is in the locked position.

Step 14. Place the cap on the Needle-Free Head, and put the ZOMA-Jet™ 10 in its carrying case until the next injection.

Important: Do not store your ZOMA-Jet™ 10 in the refrigerator.

Step 15. Place the cap on the mixed ZOMACTON™ 10 mg vial and store in an upright position in the refrigerator. See Figure Z.



Figure Z

Remove a Needle-Free Head

Each Needle-Free head must be replaced after 1 week.

- Turn the Winding Grip in the direction of “Reset” until you can see the black bar in the Dosage Window. You should be able to see the green band on the Injector Button. See Figure AA.
- Turn the Winding Grip in the direction of “Fill” until you see 0.0 in the Dosage Window. See Figure BB.
- To unlock the Needle-Free Head, turn left (counter-clockwise), then pull it straight off of the Injector Body. (If the inner part of the Needle-Free Head stays attached to the ZOMA-Jet™ 10, remove it and throw it away.)



Figure AA



Figure BB

Disposal of Your ZOMA-Jet™ 10, Needle-Free Head, and ZOMACTON™ 10 mg Vial:

- Put your used ZOMA-Jet™ 10, needle-free head, and ZOMACTON™ vial in a FDA-cleared sharps disposal container after use. Do not throw away (dispose of) your ZOMA-Jet™ 10, needle-free head, and ZOMACTON™ 10mg Vial in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
 - made of a heavy-duty plastic,
 - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
 - upright and stable during use,
 - leak-resistant, and
 - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used ZOMA-Jet™ 10, needle-free head, and ZOMACTON™ 10 mg Vial. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: <http://www.fda.gov/safesharpsdisposal>.
- Do not dispose of your used ZOMA-Jet™ 10, needle-free head, and ZOMACTON™ 10 mg Vial in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

Maintenance and Storage

ZOMACTON™ 10 mg Vial [medicine]

- Store your ZOMACTON™ 10 mg vial **upright** in a refrigerator at 36°F to 46°F (2°C to 8°C) for up to 28 days after mixing.

ZOMA-Jet™ 10 Device

- Clean the outside of your ZOMA-Jet™ 10 device with a damp cloth. **Do not** hold your device under water.
- The ZOMA-Jet™ 10 must be stored at room temperature and reset (Injector Button popped out with green band showing **and** with 0.0 showing in the Dosage Window). **Do not** store your ZOMA-Jet™ 10 device in the refrigerator.
- Stop using and contact the ZOMACTON™ patient support center if your device is not working the way it should or you notice any damage.
- The ZOMA-Jet™ 10 device can be used for about 4 years.

ZOMA-Jet™ 10 Components

- The Needle-Free Head must be replaced 1 week after opening.
- Use 1 Vial Adapter with each ZOMACTON™ 10 mg Vial.
- To order replacement Vial Adapters and Needle-Free Heads, call ZoGo Patient Support at 844.944.ZOGO (9646).
- **Do not** use your ZOMA-Jet™ 10 without Needle-Free Head attached or when Needle-Free Head is empty.

Please see enclosed full prescribing information for ZOMACTON™.

This Instructions for Use has been approved by the Food and Drug Administration.



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