Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
The dispensing of this medicine requires a doctor's prescription

ZOMACTON® 4 mg
Powder and solvent for solution for subcutaneous injection

Composition:
Each vial with powder contains:
Somatropin 4 mg
Adding 1.3 ml solvent (for use with a needle-free injection device or with a conventional syringe) produces a somatropin solution with a concentration of 3.3 mg/ml.
Adding 3.2 ml solvent (for injection only with a conventional syringe) produces a somatropin solution with a concentration of 1.3 mg/ml.

For a list of inactive ingredients and allergens in this medicine, see section 2 "Before using this medicine" and section 6 "Additional Information".

Read the entire leaflet carefully before using this medicine.
This leaflet contains concise information about this medicine. If you have further questions, refer to your doctor or pharmacist.
This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.
Use this medicine correctly. Consult a pharmacist for further information.

1. What is this medicine intended for?
Children:
- short stature due to non-secretion or inadequate secretion of pituitary growth hormone or Turner's syndrome
- short stature due to renal insufficiency.

Therapeutic group:
Somatropin is a recombinant growth hormone.

2. Before using this medicine

. . Do not use the medicine:
- If you are sensitive (allergic) to the active ingredient or to any of the other ingredients that this medicine contains.
- If you have an active malignant tumor. Malignant tumors must be inactive before beginning treatment with this medicine. You must also complete anti-cancer treatment before beginning treatment with Zomacton 4 mg.
- In children whose bone growth is completed (with closed epiphyses).
- If you have a severe illness following complications of an open heart or abdominal surgery, multiple injuries from an accident or respiratory failure.
- In children with chronic kidney disease, treatment with Zomacton 4 mg should be discontinued prior to kidney transplantation.
- In premature babies and newborns, because the solvent contains benzyl alcohol.

The solvent contains benzyl alcohol (a preservative), which may be toxic and cause allergic reactions in infants and children under 3 years old. Do not give premature babies and newborns Zomacton 4 mg.

. . Special warnings about using this medicine:
Treatment with Zomacton 4 mg must be prescribed by doctors who are specialized in treating patients with growth hormone deficiency.

- Do not use Zomacton in patients with Prader-Willi syndrome who are severely obese and/or have a history of respiratory tract diseases, unless they have a growth hormone deficiency.
- Patients who suffer from growth hormone deficiency secondary to a brain injury (intracranial lesion) must be under constant supervision for possible progression or recurrence of the underlying disease. If this condition is confirmed, your doctor will tell you whether to stop taking this medicine.
- Treatment with Zomacton 4 mg may cause low levels of thyroid hormone. This condition must be treated. Your doctor will periodically monitor your thyroid function during treatment with Zomacton 4 mg.
- Some children with growth hormone deficiency developed leukemia (a condition in which the number of white blood cells increases), unrelated to their growth hormone treatment. However, there is no evidence that incidence of leukemia in growth hormone patients is higher when there are no predisposing factors.
  No cause-and-effect relationship with growth hormone treatment has been proven.
- Pancreatitis should be considered in Zomacton 4 mg-treated children who develop abdominal pain.

Before starting treatment with Zomacton 4 mg tell your doctor if:
- You have a family history of diabetes mellitus. In this case your doctor will monitor blood sugar (glucose) levels.
- You have diabetes. Your sugar levels must be closely monitored and the dose of your sugar balancing medicines may need to be adjusted.
- You have had a serious disease such as cancer. Treatment with Zomacton 4 mg can make your illness return or get worse. If you notice any worrying symptoms consult your doctor immediately.
- You have post-surgical complications, trauma or acute respiratory failure.
- You must undergo surgery, have been seriously injured in an accident, or have a serious illness, your doctor must examine your condition carefully before recommending treatment with this medicine.

If as a result of treatment with Zomacton 4 mg you develop one of the following reactions, see a doctor or go to an emergency room immediately:
- Severe or repeated headaches.
- Problems with vision.
- Nausea and vomiting.

If you develop pain in your hip or knee, or start limping consult your doctor.

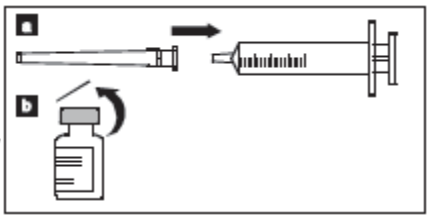
Other medicines and Zomacton 4 mg
If you are taking or have recently taken other medicines, including nonprescription medications and nutritional supplements, tell your doctor or pharmacist. In particular if you are taking:
- Steroids as a result of insufficient production of ACTH (adrenocorticotrophic hormone); steroid dose must be adjusted when given together with Zomacton 4 mg.
- High doses of androgens, estrogens, or anabolic steroids might diminish the final height.
- Prescription medicines for chronic treatment such as steroids, epilepsy medicines, and medicines for suppressing the immune system.
- Insulin, dose must be checked to ensure continued control of diabetes. Your doctor will instruct you accordingly.

Pregnancy and breastfeeding
Do not use this medicine without consulting a doctor in case of pregnancy or breastfeeding.

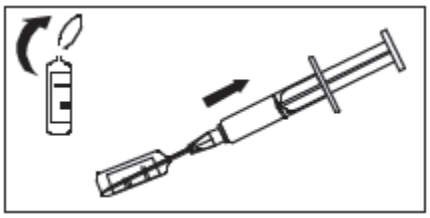
3. How to use this medicine?
Always use this medicine according to the doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how you should take this medicine.

Dosage and directions for use:
Only your doctor will determine your dose and how you should take the medicine.
Medicine is administered by subcutaneous injection (under the skin).
The medicine can be injected with the ZomaJet needle-free injection device, or, alternatively, using a conventional syringe.
Instructions for use with the needle-free device are provided in the instruction manual supplied with the device.
Dosage is individual and calibrated for each patient.
To prevent atrophy of the fatty layer under the skin, it is advisable to periodically vary the injection site.

Instructions for preparing Zomacton 4 mg growth hormone solution:

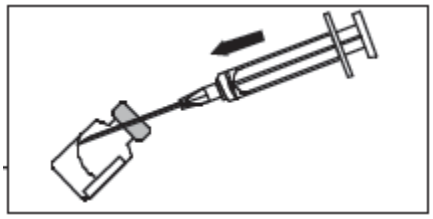


1a. Fit the needle onto the graduated syringe.
1b. Remove the hard plastic cover from the Zomacton 4 mg vial (the vial with the white powder) and clean the stopper that is left on the vial with an alcohol swab.

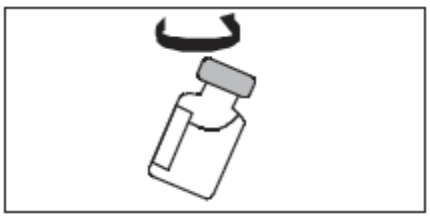


2. Snap off the top of the solvent ampoule. Remove the plastic cover on the needle. Make sure that the plunger is completely pushed in before introducing the needle into the ampoule. Slowly draw up the required volume in the syringe.

Your doctor will tell you whether to use 1.3 ml or 3.2 ml of solvent:
Adding 1.3 ml solvent produces a solution with a concentration of 3.3 mg/ml (for use with a ZomaJet needle-free injection device or a conventional syringe).
Adding 3.2 ml solvent produces a solution with a concentration of 1.3 mg/ml (for use with a conventional syringe only).



3. Insert the syringe with solvent into the center of the rubber stopper on the Zomacton 4 mg vial and inject the solvent slowly, aiming the stream of liquid against the wall of the vial in order to prevent foaming.



4. Take the syringe out of the vial. Swirl the contents of the Zomacton 4 mg vial with a **gentle** rotary motion until completely dissolved and you have a clear solution. **Do not shake vigorously.** Shaking vigorously can cause cloudiness.
After reconstitution, the contents of the vial must be clear and free of particles. If the solution is cloudy or there are particles in it, **do not inject it**.

Occasionally, refrigerating Zomacton 4 mg growth hormone solution may cause some cloudiness of the solution. If this happens, leave the vial outside the refrigerator until it reaches room temperature. If the solution remains cloudy or there are particles in it, **do not use it.**

Do not exceed the recommended dose.

If you have accidentally taken an overdose, or if a child has accidentally swallowed some medicine, go immediately to a doctor or a hospital emergency room and bring the medicine package with you. A Zomacton 4 mg overdose can cause a drop in blood sugar level (hypoglycemia) and then a rise in blood sugar level (hyperglycemia). Repeated Zomacton 4 mg overdose may have an unpredictable effect.

If you forget to take this medicine at the scheduled time, do not take a double dose. Take the next dose at the usual time and consult your doctor.

Persist with the treatment as recommended by your doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor or pharmacist.
Do not take medicines in the dark! Check the label and dose every time you take a medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or the pharmacist.

4. Side effects

Like all medicines, using Zomacton 4 mg may cause side effects in some people. Do not be alarmed by this list of side effects. You may not experience any of them.
Injecting growth hormone under the skin may reduce or raise fat levels at the injection site; there may also be bleeding which will appear as spots and bruises on the skin (purple marks on the skin) at the injection site. It is therefore advisable to frequently change the injection site. In rare cases patients may develop pain or an itchy rash at the injection site.

Very common side effects (appear in more than one user out of ten)
Adults only:
- Edema caused by fluid build-up mainly in the hands and feet.
- Slight rise in blood sugar level (hyperglycemia).
- Joint pain (arthralgia).
- Muscle pain (myalgia).
- Headache.
- Numbness, tingling, burning, or creeping sensation (paresthesia) on the skin.

Common side effects (appear in 1-10 users out of 100)
Children and adults:
- Hypothyroidism.
- Immune reaction to growth hormone; can be detected in a lab test by the presence of growth hormone antibodies.
- Headache.
- Increased muscle tone (hypertonia).

Children only:
- Edema caused by fluid build-up mainly in the hands and feet.
- Reactions at the injection site.

- Weakness.
- Glucose intolerance.
- Joint pain.
- Muscle pain.

Adults only:
- Stiffness in the arms and/or legs.
- Difficulty falling asleep or sleep disorders (insomnia).

Uncommon side effects (appear in 1-10 users out of 1,000)
Adults and children:
- Anemia.
- Fast heart rate (tachycardia).
- Dizziness (vertigo).
- Double vision (diplopia).
- Edema of the optic nerve head (papilloedema).
- Vomiting, flatulence, stomach ache, nausea.
- Weakness.
- Atrophy (thinning) of tissue at the injection site, bleeding in the injection site, lump at the injection site, thickening of tissue at the injection site (hypertrophy).
- Decline in blood sugar level (hypoglycemia).
- Rise in phosphorus level (hyperphosphatemia).
- Muscle atrophy.
- Bone pain.
- Carpal tunnel syndrome.
- Malignant tumors.
- Sleepiness.
- Involuntary eye movement (nystagmus).
- Personality disorders.
- Urinary incontinence, blood in the urine, excessive volume of urine (polyuria), increased frequency of urination, and abnormal urination.
- Discharge from genitals.
- Side effects at the injection site (such as: thinning of the fatty layer under the skin, skin atrophy, skin irritation, allergic skin reaction (urticaria), excessive body hair, excessive skin proliferation (hypertrophy)).

Children only:
- Stiffness in hands and legs.

Adults only:
- Hypertension.
- Enlarged breasts in men (gynecomastia)

Rare side effects (appear in 1-10 users out of 10,000)
Adults and children:
- Diarrhea.
- Abnormal results in kidney function test.
- Type II diabetes.
- Prickling or numbness in certain parts of the body (neuropathy).
- Increased intracranial pressure (presents as severe headache, blurred vision, nausea and vomiting).

Children only:
- Hypertension.
- Difficulty falling asleep, sleep disorders (insomnia).
- Numbness, tingling, burning or creeping sensation on the skin (paresthesia).

Very rare side effects (appear in less than one user out of 10,000)

Children only:

- Leukemia (disease incidence among children is not greater than its incidence in the general population).
- Enlarged breasts in boys (gynecomastia).

If you experience any side-effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects
You can report side effects to the Ministry of Health (MoH) by following the link 'Reporting Side Effects of Medication' on the MoH home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

5. How to Store the Medicine?

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor!
- Do not use this medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of that month.

Storage: At a temperature of 2°-8°C (in the refrigerator), before and after reconstitution. After reconstitution, Zomacton 4 mg should be used within 14 days.

6. Additional information

In addition to the active ingredient this medicine also contains:
sodium chloride, benzyl alcohol, mannitol, water for injection.
The solvent contains 9 mg/ml of benzyl alcohol.

What the medicine looks like and what are the contents of the package:
This medicine package contains:
One vial with a white powder and one ampule with solvent.

Manufacturer: Ferring GmbH, Kiel, Germany.
License holder: Ferring Pharmaceuticals Ltd., 8 Hashita St., Ind. Park Caesarea 3088900.

This leaflet was reviewed and approved by the Ministry of Health in December 2016 and revised in July 2019 in accordance with Ministry of Health guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 032-64-25442.