Package leaflet: Information for the user

Humatrope® 6 mg/ 12 mg/ 24 mg powder and solvent for solution for injection
Somatropin

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Humatrope is and what it is used for

Your medicine or the medicine of the person in your care is called Humatrope. It contains human growth hormone, also called somatropin. Humatrope is made by a special process known as recombinant DNA technology. It has the same structure as the growth hormone that your body produces.

Growth hormone regulates the growth and development of cells in your body. When it stimulates growth of cells in the spine and in the long bones of the legs, it causes an increase in height.
In growth hormone deficiency, growth hormone also increases the bone mineral content, the number and size of the muscle cells and reduces the body fat stores.

Humatrope is used for
- Treatment of children and adolescents with any of the following growth disorders:
  - Insufficient production of growth hormone (Growth hormone deficiency),
  - Absence of all or some of the X-sex chromosomes in females with short stature (Turner syndrome),
  - A condition in which the kidneys are damaged (chronic problems with the way the kidneys work) in children before puberty with growth retardation,
  - Small at birth (SGA = Small for gestational age) with failure to catch-up height by 4 years of age or later,
  - An alteration to a gene called SHOX (SHOX deficiency).
- Treatment of adults who have confirmed growth hormone deficiency beginning in either childhood or adulthood.

2. What you need to know before you use Humatrope

Do not use Humatrope
- if you are **allergic** (hypersensitive) to somatropin or any of the other ingredients of Humatrope (e.g. metacresol, glycerol in the solvent), see section 6.

- and tell your doctor if you have an active tumour (cancer). Tumours must be inactive and you must have finished your anti-tumour treatment before you start your treatment with Humatrope.
- if you have **already stopped growing** and want to promote further growth in height (closed growth plates at the end of long bones). Your doctor will examine you to decide if you still require Humatrope after your bones have stopped growing.
- if you are **very ill** and require intensive medical care for a serious heart or abdominal operation, being treated for multiple injuries from an accident, or require mechanical breathing treatment following acute lung failure.

Warnings and Precautions
Talk to your doctor or pharmacist before using Humatrope.

If you have been treated for growth hormone deficiency during childhood, your doctor will re-examine you for growth hormone deficiency to decide if you require further Humatrope treatment during adulthood.

If you have completed previous anti-tumour therapy, a scan of your brain may be required before the start of Humatrope treatment. You should be examined regularly to make sure that the tumour does not come back or start growing.

A higher risk for having a second tumour (benign and malignant) has been reported in patients that survived their cancer and were treated with somatropin. Of these second tumours, in particular, brain tumours were the most common.

If you have symptoms such as frequent or bad headache, with nausea and/or vision problems occur, tell your doctor immediately. Your doctor should perform an examination of the eyes to look for evidence of increased brain pressure. Depending on the results of this examination, treatment with Humatrope may have to be interrupted.

If you develop a limp or pain in the hip, please ask your doctor for advice. During periods of growth, you may develop bone disorders in your hips.

If you start treatment, Humatrope can affect the amount of thyroid hormones in your blood. If the thyroid hormone level is low, it may reduce your response to Humatrope. Therefore, you must have regular thyroid function tests regardless whether you receive thyroid hormone therapy or not.

If you are a child, make sure that you continue treatment until the end of growth has been reached.

If you take a higher than prescribed dose of Humatrope, you may experience overgrowth of some parts of your body such as ears, nose, jaw, hands and feet. Overdose may also lead to increased levels of blood sugar and sugar in the urine. Always use Humatrope as recommended by your doctor.

If you have growth disorder due to kidney damage, treatment with Humatrope should be stopped prior to kidney transplantation.

If you have acute critical illness, your treating doctor should be notified. Deaths have been reported in patients receiving somatropin during critical illness.

If you are growth hormone deficient and also have Prader-Willi syndrome (a genetic disorder), your doctor should examine you for breathing problems and airway infections before starting Humatrope treatment, especially if you are overweight, have previously experienced severe breathing problems (especially during sleep), or suffered infection of the lungs or airways. If during treatment you have signs of breathing problems (snoring), treatment should be interrupted and the cause assessed by your doctor.

Humatrope may affect the way your body handles sugar from food and drink by interfering with the way your body uses insulin. Therefore, if you take Humatrope, your doctor should check if your body is dealing with the sugars correctly.
If you have diabetes mellitus, your insulin dose may need to be adjusted after starting Humatrope treatment. Your doctor will check the amount of sugar in your blood and may adjust your diabetes therapy.

If you have a growth disorder associated with being born small for gestational age, your blood sugar and insulin levels will be checked before starting the treatment and regularly during treatment.

Elderly patients (over 65 years) may be more sensitive to Humatrope and may be prone to side effects.

Children who are treated with somatropin have an increased risk of developing an inflammation of the pancreas (pancreatitis) compared to adults treated with somatropin. Although rare, pancreatitis should be considered in somatropin-treated children who develop abdominal pain.

Scoliosis (an increase in sideways curvature of the spine) may progress in any child during rapid growth. Signs of scoliosis should be monitored during treatment.

Other medicines and Humatrope
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines and especially any of the following medicines:

- medicines for the treatment of **diabetes mellitus** which may have to be adjusted.
- **adrenal steroid hormone** (glucocorticoid), such as cortisone or prednisolone; your doctor may need to adjust the dose because the combination of these medicines with Humatrope may reduce the effect of both treatments.
- **oestrogen replacement therapy**, as it may affect the response to growth hormone treatment. If there is a change to the way oestrogen is taken (e.g. oral to transdermal: through the skin); Humatrope dose may need to be adjusted.
- medicines to prevent seizure (**anticonvulsants**) or cyclosporine.

Pregnancy and breast feeding
Humatrope should not be used during pregnancy, unless your doctor tells you to do so. If you become pregnant, tell your doctor immediately.
It is not known whether somatropin enters the breast milk. If you are breast-feeding, or intend to breast-feed, please ask your doctor for advice before using Humatrope.
Driving and using machines
Humatrope has no known effect on ability to drive or use machines.

Humatrope contains sodium
Humatrope contains less than 1 mmol per daily dose of sodium, it is therefore considered essentially sodium-free.

3. How to use Humatrope

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

- Always make sure you use the strength of cartridge your doctor prescribed (either 6 mg, 12 mg or 24 mg strength) and the appropriate CE-marked Humatrope pen injection system. Never use cartridges of other medicines in your Humatrope pen.
- Each cartridge of Humatrope comes with a syringe containing a diluent (solvent for solution for injection) for reconstitution (mixing and preparing of the injection solution).
- You must not mix or inject Humatrope until you have received appropriate training from your doctor or other qualified health care professionals.

- For detailed instructions on how prepare and inject Humatrope, please see Section "**How to inject Humatrope**" at the end of this leaflet. You must only mix Humatrope with the diluent provided. Never mix it with anything else unless your doctor tells you to.
- After reconstitution, Humatrope should be injected into the fat tissue just beneath the skin using a short needle and a pen injection system.
- The injection sites should be varied in order to avoid local reduction and hardening of the fat tissue under the skin (lipoatrophy).
- After mixing Humatrope, do not leave it out of the refrigerator for longer than 30 minutes each day.
- Keep your pen with the rest of the Humatrope in the fridge. Do not use any Humatrope left over in the pen after 28 days of mixing.

Dosage
Your doctor will advise you on your dosage and administration schedule. Do not change your dosage without talking to your doctor.
Usually, treatment with Humatrope is a long term treatment; your doctor may need to adjust your dose over time depending on your body weight and response to treatment. In general, the dose is calculated according to the following recommendations and administered once daily:

Children and adolescents with:
- ***Growth hormone deficiency:***
  0.025–0.035 mg/kg body weight daily,
- ***Turner syndrome:***
  0.045–0.050 mg/kg body weight daily,
- ***Chronic problems with the way the kidneys work:***
  0.045–0.050 mg/kg body weight daily,
- ***Small for gestational age at birth:***
  0.035 mg/kg body weight daily. Treatment should be discontinued after the first year of treatment if the growth rate is insufficient,
- ***SHOX gene deficiency:***
  0.045-0.050 mg/kg body weight daily.

Growth hormone deficiency in adults:
Treatment should be started with a low dose of 0.15–0.30 mg daily. Lower starting doses may be required in older and overweight patients. The starting dose may be increased gradually according to your individual requirements. Total daily dose usually does not exceed 1 mg.
Dose requirements may decline with increasing age. Women, especially those on oral oestrogen replacement, may require higher doses than men.

If you use more Humatrope than you should
If you have injected more Humatrope than you should have, please ask your doctor for advice.
- If you have injected too much Humatrope, initially your blood sugar may decrease and become too low (hypoglycaemia) and subsequently increase and become too high (hyperglycaemia).
- If you inject too much Humatrope over a longer period (years), you may experience overgrowth of some parts of your body such as ears, nose, jaw, hands and feet (acromegaly).

If you forget to use Humatrope
Do not inject a double dose to make up for a forgotten dose. Continue with the prescribed dosage. If you forget to inject Humatrope and have any doubts about what to do, please contact your doctor.

If you stop using Humatrope
Please ask your doctor for advice before stopping treatment. Interruption or early stopping of treatment with Humatrope may impair the success of the Humatrope treatment.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
You may experience any of the following side effects after injecting Humatrope:

The following convention has been used for the classification of the adverse reactions:
Very common side effects may happen in more than 1 in 10 patients
Common side effects may happen in 1 in 100 to 1 in 10 patients
Uncommon side effects may happen in 1 in 1,000 to 1 in 100 patients
Rare side effects may happen in 1 in 10,000 to 1 in 1,000 patients
Very rare side effects may happen in fewer than 1 in 10,000 patients, including isolated reports
Other possible side effects (frequency cannot be estimated from the available data)

Children				
Common	**Uncommon**	**Rare**	**Very rare**	**Other**
Injection site pain Swelling (Oedema) High blood sugar (hyperglycaemia) Hypersensitivity to metacresol or/and glycerol Low levels of thyroid hormone Development of anti-growth hormone antibodies Progression of scoliosis (an increase in sideways curvature of the spine)	Weakness Type 2 diabetes mellitus	Bad or frequent headaches with nausea and/or vision problems are signs of increased brain pressure (benign intracranial hypertension). Tell your doctor immediately if this happens. Numbness and tingling (paraesthesia) Localised muscle pain (myalgia)	Difficulties sleeping (insomnia) High blood pressure (hypertension) Breast enlargement (gynaecomastia) Sugar in urine (glucosuria)	Hypersensitivity to active substance

Adults				
Very common	**Common**	**Uncommon**	**Rare**	**Other**
Headache Joint pain (arthralgia)	Injection site pain Swelling (Oedema) High blood sugar (hyperglycaemia) Hypersensitivity to metacresol or/and glycerol Low levels of thyroid hormone Difficulties sleeping (insomnia) Numbness and tingling (paraesthesia) Numbness and tingling in fingers and palm of the hand due to squeezed nerve at hand wrist (carpal tunnel syndrome) Localised muscle pain (myalgia) High blood pressure (hypertension) Shortness of breath (Dyspneoa) Temporary interruption of breathing during sleep (Sleep Apneoa)	Weakness Breast enlargement (gynaecomastia)	Bad or frequent headaches with nausea and/or vision problems are signs of increased brain pressure (benign intracranial hypertension). Tell your doctor immediately if this happens. Sugar in urine (glucosuria**)**	Type 2 diabetes mellitus Hypersensitivity to active substance

The effect of insulin may be reduced.

Leukaemia has been reported in a small number of children who have been treated with growth hormone. However there is no proof that leukaemia occurrence is elevated in patients receiving growth hormone.

Reporting of side effects
If you get any of the side effects, talk to your doctor or pharmacist. This includes any side effects not listed in this leaflet.
You can also report side effects directly via **UK**: Yellow Card Scheme, website: www.mhra.gov.uk/yellowcard, **Malta**: ADR Reporting, website: www.medicinesauthority.gov.mt/adrportal. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Humatrope

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and carton. The expiry date (EXP) refers to the last day of the month.

Do not use this medicine if you notice that the solution is cloudy or has any particles in it.

Always store Humatrope in a refrigerator (2°C – 8°C). Do not freeze.

After mixing Humatrope, do not leave it out of the refrigerator for longer than 30 minutes each day. Humatrope can be used for up to 28 days after mixing if you keep it in the fridge and no longer than 30 minutes each day at room temperature.

Do not throw away any medicines via waste water or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Content of the pack and other information

What Humatrope contains

Powder in a cartridge
The active substance is somatropin. Each cartridge contains 6 mg, 12 mg or 24 mg depending on the strength. When reconstituted:

- **Humatrope 6 mg** gives 2.08 mg somatropin per ml solution
- **Humatrope 12 mg** gives 4.17 mg somatropin per ml solution
- **Humatrope 24 mg** gives 8.33 mg somatropin per ml solution

The other ingredients are: mannitol, glycine, dibasic sodium phosphate.
[Phosphoric acid or sodium hydroxide (or both) may have been used in the manufacturing process to adjust acidity].

Sterile Diluent Syringe
The pre-filled solvent syringe contains: glycerol, metacresol, water for injection. [Hydrochloric acid or sodium hydroxide (or both) may have been used in the manufacturing process to adjust acidity].

What Humatrope looks like and contents of the pack

Humatrope 6 mg:	• 1 cartridge with white powder for solution for injection, • 3.17 ml of clear colourless solvent solution in a pre-filled syringe Pack size of 1, 5 and 10
Humatrope 12 mg:	• 1 cartridge with white powder for solution for injection, • 3.15 ml of clear colourless solvent solution in a pre-filled syringe Pack size of 1, 5 and 10
Humatrope 24 mg:	• 1 cartridge with white powder for solution for injection, • 3.15 ml of clear colourless solvent solution in a pre-filled syringe. Pack size of 1, 5 and 10

Not all pack sizes may be available in your country

Marketing Authorisation Holder
Eli Lilly and Company Limited
Lilly House, Priestley Road
Basingstoke, Hampshire
RG24 9NL, United Kingdom

Manufacturer
Lilly France
Rue du Colonel Lilly
F-67640 Fegersheim
France

For any information about this medicine, please contact the Marketing Authorisation Holder (or the local representative):
Eli Lilly and Company Limited, Lilly House, Priestley Road, Basingstoke, Hampshire, RG24 9NL, United Kingdom. Phone: +44 (0) 1256 315000.

This medicinal product is authorised in the Member States of the EEA under the following names:
In member states of the EEA where this medicinal product is authorized, it is authorized under the name "Humatrope", except in France where it is authorized under "Umatrope”.

How to inject Humatrope 6 mg/ 12 mg/ 24 mg

The following instructions explain how to inject Humatrope. Please read the instructions carefully and follow them step by step.

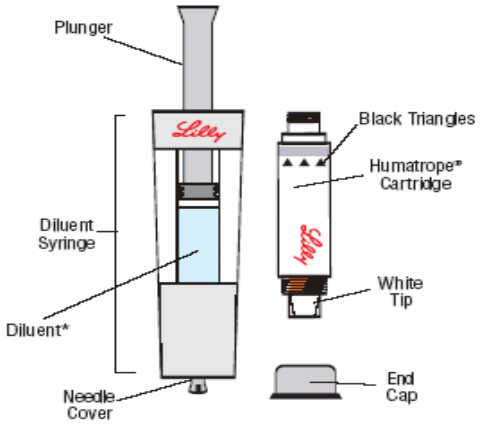
Getting started:

You will require five items:

1. Humatrope cartridge of the correct strength
2. A syringe filled with diluent
3. A CE-marked Humatrope pen
4. A sterile pen needle, and
5. An alcohol swab

Wash your hands before you continue with the next steps

Parts



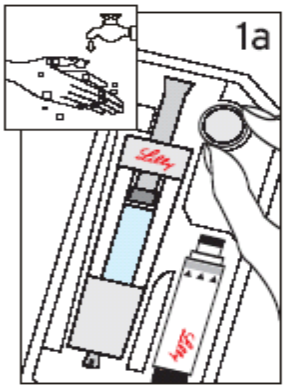
Only use parts from this kit to prepare the drug cartridge.

*Note: The liquid is colourless. It is shown here as blue for illustration purposes only.

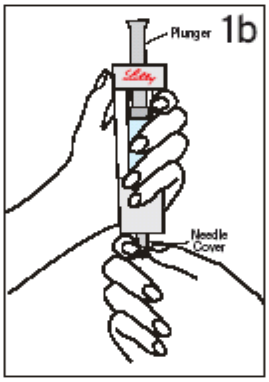
The following steps will guide you to prepare your new cartridge for use

Step 1 Unpacking

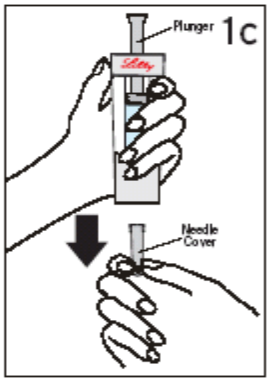
- You must only mix Humatrope with the diluent provided. Never mix it with anything else unless your doctor tells you to.
- Please read the user manual that comes with your pen. This will remind you what you have been taught by your doctor or health care professional.
- Please follow the instruction underneath the diagrams



Remove **ALL** contents from the tray. Note: This product is designed for left or right handed use. Please feel free to use whichever hand is most comfortable for you.

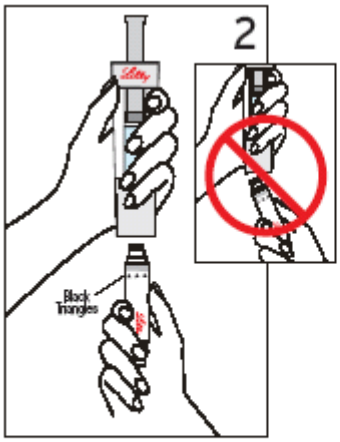


Grasp Needle Cover, which is at the bottom of the Diluent Syringe.

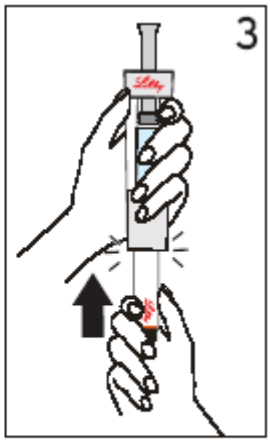


Remove Needle Cover and discard. **DO NOT** depress Plunger yet. It is okay if a drop of fluid is lost. It is not necessary to release air from the Diluent Syringe.

Step 2&3 Connecting the cartridge

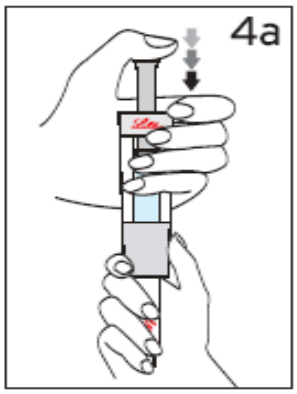


Hold cartridge, Black Triangles up. Align the cartridge and Diluent Syringe in a straight line. **DO NOT** insert the cartridge at an angle.

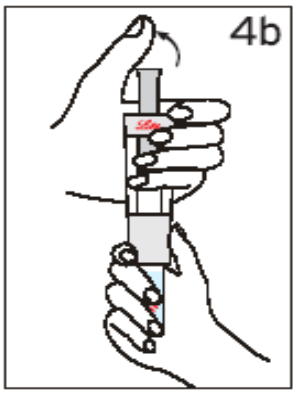


PUSH the cartridge **STRAIGHT** in until it stops **AND** the Black Triangles **ARE COVERED**. You may hear or feel a click. **DO NOT** twist the cartridge.

Step 4 Mixing Humatrope

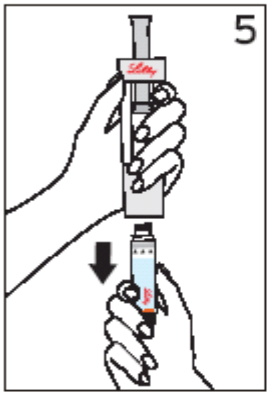


Hold the Diluent Syringe and the cartridge together with **TWO HANDS**. Push and release the Plunger 2 or 3 times until the Diluent is in the cartridge.

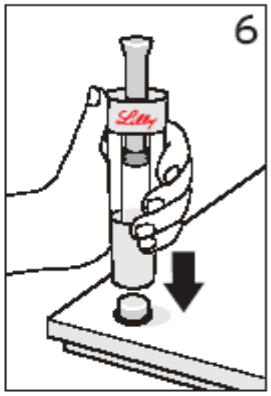


Remove thumb from the Plunger and check that the Diluent Syringe is empty (it is normal for small drops of Diluent to remain in the Diluent Syringe).

Step 5&6 Release Cartridge and Discard Diluent



With thumb **OFF** the plunger, pull the cartridge from the Diluent Syringe.

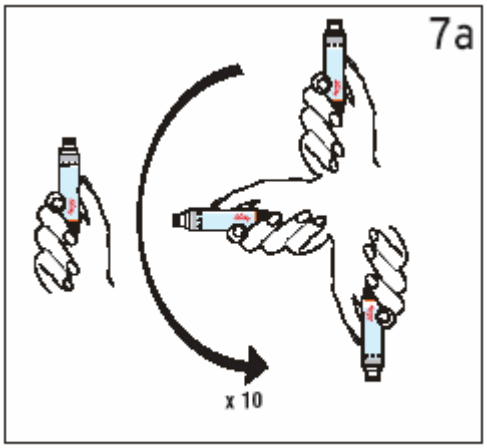


Place the End Cap on a hard, flat surface. Push the Diluent Syringe onto the End Cap and immediately discard the Diluent Syringe as instructed by your healthcare professional.

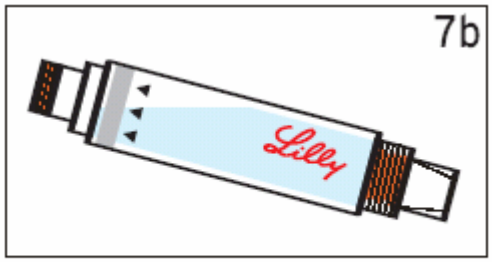
Step 7 Gently Mix

- Mix the solution by gently rotating the cartridge 10 times. DO NOT SHAKE THE CARTRIDGE. Let the cartridge sit for 3 minutes, then inspect the solution carefully.

- If the solution is cloudy or contains particles, gently mix the cartridge another 10 times. Let the cartridge sit for 5 more minutes. If the solution remains cloudy or contains particles DO NOT USE THE CARTRIDGE.



Gently mix the cartridge 10 times and let sit for 3 minutes, DO NOT SHAKE.



Inspect the solution. The Humatrope® solution should be clear.

<u>Step 8 Injecting Humatrope using a suitable pen injection system</u>

- If the solution is clear, your cartridge is now ready to be attached to the suitable Humatrope pen.
- Put the cartridge in the pen (see the user manual for the pen).
- Always use a new sterile needle for each injection.
- Wipe the skin thoroughly with an alcohol swab. Let the skin dry.
- Set the correct dose (see the user manual of the pen).
- Inject slowly under the skin (subcutaneous) in the way you have been taught by your doctor.
- Remove the needle from the skin and safely dispose of the needle, as you have been shown by your doctor or health care professional.
- Keep your pen with the rest of the Humatrope in the fridge. Do not use any Humatrope left over in the pen after 28 days of mixing.

Humatrope is a trademark of Eli Lilly and Company Limited

This leaflet was last revised in November 2016.