

Package leaflet: Information for the user

MERCK

saizen® 8 mg/ml 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 symptoms 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 Saizen is and what it is used for
2. What you need to know before you use Saizen
3. How to use Saizen
4. Possible side effects
5. How to store Saizen
6. Contents of the pack and other information

1. What Saizen is and what it is used for

Saizen is a growth hormone. Saizen's main action is to increase growth in children and adolescents and to treat adults with growth hormone deficiency.

The growth hormone (somatropin) contained in Saizen is almost the same as human's natural growth hormone except that it is made outside the body by a process called "recombinant DNA technology" (genetic engineering).

Saizen is used:

In children and adolescents:

- in the treatment of children with short stature who have failed to grow because their body produces no growth hormone or insufficient levels of growth hormone
- in the treatment of girls who have failed to grow due to gonadal dysgenesis (also referred to as Turner syndrome), confirmed by a test on the chromosomes
- in the treatment of pre-pubertal children who have failed to grow due to chronic renal failure, a condition in which kidneys are damaged
- in the treatment of growth problems in children who were born small and who have not reached normal height by the age of 4 years or later.

In adults:

- in the treatment of adults with a marked lack of growth hormone (growth hormone deficiency).

This therapy is given to adults who have a serious growth hormone deficiency that has been medically diagnosed by a test.

The doctor or pharmacist will be able to explain why this medicine has been given to you or to your child.

2. What you need to know before you use Saizen

Do not use Saizen

- If you (or your child) are allergic (hypersensitive) to somatropin or any of the other ingredients of this medicine (listed in section 6).
- If you have been told that your child's bones have stopped growing and that he/she has therefore reached his/her final height.
- 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 Saizen.
- If you (or your child) have diabetes and are suffering from an associated eye disease (proliferative or preproliferative diabetic retinopathy).
- If you or your child have an acute critical illness, suffering complications following open heart surgery, abdominal surgery, multiple accidental trauma, acute respiratory failure or similar conditions.

Treatment with Saizen has to be stopped in children with chronic kidney disease at time of kidney transplantation.

Warnings and precautions

Talk to your doctor before using Saizen.

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

Shortly after Saizen is given, you (or your child) may feel shaky or light-headed due to low blood sugar levels. These feelings will quickly disappear. Your (or your child's) blood sugar levels may then rise above normal 2-4 hours after administration. Since treatment with growth hormone can alter how your body handles sugar, your (or your child's) sugar levels will be tested regularly by a doctor. Somatropin may cause your (or your child's) blood sugar to increase. If you (or your child) are diabetic or a member of your family has diabetes, your doctor will monitor closely your blood sugar level and may adjust the treatment for diabetes while you are being treated with Saizen. Please be aware that you may need regular eye tests after having this medicine.

Saizen may affect how your thyroid works. Your doctor may test your blood for levels of thyroid hormones and prescribe another hormone if you (or your child) are found to have developed a lack of thyroid hormone.

If you (or your child) are using corticosteroids, you should consult your doctor regularly, as you may need adjustment of your corticosteroid or your Saizen dose.

Saizen may cause fluid retention in adult patients. This may appear as swelling and joint or muscle pain. If you feel these symptoms tell your doctor who may decide to adjust your dose of Saizen.

If you have had a tumour in your childhood and were treated with Saizen, there is an increased risk to develop a new tumour. If in the past you (or your child) have had a condition affecting the brain, e.g. a tumour, the doctor will examine you (or your child) regularly to check that this has not come back again.

Rarely Saizen may cause an inflammation of the pancreas, which causes severe pain in the abdomen and back. Please consider this especially if your child suffers from stomach ache and contact your doctor. An increase in sideways curvature of the spine (scoliosis) may progress in any child during rapid growth. During treatment with Saizen, your doctor will check you (or your child) for signs of scoliosis.

Some patients may develop swelling of the brain, while taking Saizen. If you (or your child) suffer from a bad or recurrent headache, problems with your eyesight, feel sick (nausea) and/or being sick (vomiting), contact your doctor immediately. In this case it may be necessary to stop the growth hormone treatment, although treatment may be re-started at a later date. If the symptoms of brain swelling come back, treatment with Saizen should be discontinued.

When the medicine is injected into the same place over a long period of time, it can cause damage to this area. It is therefore important to keep changing the injection site. Your doctor or pharmacist can speak to you about which parts of the body should be used (see section 3 How to use Saizen).

Some children with growth hormone deficiency have developed leukaemia (increased number of white blood cells), whether or not they have received treatment with growth hormone. However there is no evidence that leukaemia incidence is increased in growth hormone recipients without predisposing factors. No cause and effect relationship with growth hormone treatment has been proven.

Hip problems may occur more commonly in children with hormone or kidney problems. If your child has chronic renal failure, which can occur

when kidneys are damaged, he or she should be examined periodically for evidence of bone disease. It is uncertain whether the bone disease in children with hormone or kidney problems is affected by growth hormone therapy. X-rays of the hip should be obtained prior to initiating therapy. If your child develops a limp or complains of hip or knee pain while being treated with Saizen, tell your doctor.

Treatment with Saizen will be stopped in children with chronic kidney failure at the time of kidney transplant.

Saizen is not indicated for the long-term treatment of paediatric patients who have growth failure due to genetically confirmed Prader-Willi syndrome, unless they also have a diagnosis of growth hormone deficiency. There have been reports of sleep apnoea and sudden death after initiating therapy with growth hormone in paediatric patients with Prader-Willi syndrome who had one or more of the following risk factors: severe obesity, history of upper airway obstruction or sleep apnoea, or unidentified respiratory infection.

Growth hormone should generally not be used by people who are seriously ill.

If you do not respond to the therapy with Saizen, you may have developed antibodies to growth hormone. Your doctor will conduct appropriate tests to determine this.

If you are over 60 years old or if you are taking Saizen for a long time you should be examined more frequently by your doctor. As there is less experience both in the treatment of older people and in prolonged treatment with Saizen, special care is required.

Other medicines and Saizen

Tell your doctor or pharmacist if you (or your child) are using, have recently used or might use any other medicines.

If you (or your child) are using corticosteroids, it is important to tell the doctor or pharmacist. These medicines could interact with Saizen and therefore your doctor may need to adjust the dose of these medicines or your Saizen dose. Corticosteroids are used to treat several illnesses including asthma, allergies, kidney rejection and rheumatoid arthritis.

If you have a replacement therapy with oral oestrogens, it may reduce the effect of Saizen on growth. Therefore your doctor may need to adjust your Saizen dose.

If you are treated with sex hormones, medicines to control epilepsy (anticonvulsants) or cyclosporine (a medicine that weakens the immune system after transplantation), you should tell your doctor as the dose of these medicines may need to be adjusted.

Pregnancy and breast feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

There is currently insufficient evidence from human studies on the safety of growth hormone treatment during pregnancy and breast feeding. Saizen should be discontinued, if pregnancy occurs.

Driving and using machines

No studies on the effects of Saizen on the ability to drive and use machines have been performed.

Somatropin-containing products have no influence on the ability to drive and use machines.

Important information about some of the ingredients of Saizen

This medicine contains less than 1 mmol sodium (23 mg) per reconstituted solution, that is to say essentially 'sodium-free'.

3. How to use Saizen

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

Dosage

The dose and frequency of administration of Saizen will be decided by your doctor and will depend on your (or your child's) body weight or body surface area.

It is recommended that Saizen be administered at bedtime.

Children and adolescents:

- Short stature due to a lack of, or insufficient levels of natural growth hormone:
0.7-1.0 mg/m² body surface area each day or 0.025-0.035 mg/kg body weight each day by subcutaneous administration (under the skin)
- Growth failure in girls due to gonadal dysgenesis (Turner syndrome):
1.4 mg/m² body surface area per day or 0.045-0.050 mg/kg body weight each day by subcutaneous administration (under the skin).

If your daughter is treated for Turner syndrome and she receives non-androgenic anabolic steroids as well, growth response may be enhanced. Ask your doctor or pharmacist if you are not sure about these drugs.

- Growth failure in pre-pubertal children due to chronic renal failure, a condition in which kidneys are damaged:
1.4 mg/m² body surface area, approximately equal to 0.045-0.050 mg/kg body weight each day by subcutaneous administration (under the skin).
- Growth problems in children who were born small:
1 mg/m² body surface area, approximately equal to 0.035 mg/kg body weight each day by subcutaneous administration (under the skin).

Adults:

- Growth hormone deficiency in adults

At the start, low doses of 0.15-0.30 mg each day are recommended by subcutaneous injection (under the skin). The dose will be adjusted in stages by your doctor. The recommended final dose of growth hormone rarely exceeds 1.0 mg/day. In general the lowest efficacious dose that works for you should be administered. If you are older or overweight, a lower dose may be necessary.

Method and route of administration

The dose and frequency of administration of Saizen will be decided by your doctor and will depend on your (or your child's) size or body weight. In general Saizen should be administered each day by subcutaneous injection (under the skin).

Important information

For administration of Saizen, please read the following instructions carefully.

When the medicine is injected into the same place every time for a long time, it can cause damage. It is important to keep changing the place where you have your injection. Your doctor or pharmacist can speak to you about which part of the body you should use. Do not use any areas in which you feel lumps, firm knots, depressions, or pain; talk to your doctor or pharmacist about anything you find. Clean the skin at the injection site with soap and water.

The cartridge containing the solution of Saizen is ready to be used for administration with your cool.click needle-free auto-injectors, easypod auto-injector or aluetta pen injectors.

Each Saizen cartridge presentation is colour coded and must be used with the matching colour coded aluetta pen injector to give the correct dose. The cartridge containing 12 mg somatotropin (red) must be used with the aluetta pen injector 12 (red). The cartridge containing 20 mg somatotropin (yellow) must be used with the aluetta pen injector 20 (yellow).

Place all elements needed for the injection of the solution on a clean surface and wash your hands with soap and water.

The solution should be clear to slightly opalescent with no particles and without visible signs of deterioration. If the solution contains particles, it must not be injected.

How to perform your daily self-administration of Saizen

For instructions on how to load the cartridge into the cool.click needle-free auto-injectors, easypod auto-injector or aluetta pen injectors and inject

the solution of Saizen, please carefully read the corresponding instruction manual provided with each injector. Intended users of easypod are primarily children starting from the age of 7 up to adults. Use of the devices by children should always be made under adult's supervision.

Duration of treatment

Your child should stop using this treatment when he or she reaches a satisfactory adult height or his or her bones cannot grow any longer, as assessed by his or her doctor. Treatment with Saizen will be stopped in children with chronic kidney failure at the time of kidney transplant.

In adults a lack of growth hormone is a lifelong condition and it should be treated accordingly by your doctor.

If you use more Saizen than you should

If you inject too much Saizen, you should tell your doctor as it may be necessary to change slightly the dose to make up for this. Injecting too much can lead to changes in blood sugar levels which could mean that you (or your child) will feel shaky and light-headed. If this happens contact your doctor as soon as possible.

If you forget to use Saizen

If you miss a dose, tell your doctor as it may be necessary to slightly change the dose to make up for this.

If you stop taking Saizen

Do not stop taking Saizen without speaking with your doctor.

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.

Tell your doctor immediately if you experience strong and recurrent headaches associated with feeling sick (nausea), vomiting or sight disturbances. These are symptoms of a side effect called benign intracranial hypertension and it is uncommon.

Side effects may occur with certain frequencies, which are defined as follows:

- very common: may affect more than 1 in 10 people
- common: may affect up to 1 in 10 people
- uncommon: may affect up to 1 in 100 people
- rare: may affect up to 1 in 1,000 people
- very rare: may affect up to 1 in 10,000 people
- not known: frequency cannot be estimated from the available data.

Common side effects:

- Reactions at the injection site such as e.g. redness, itching, swelling, rash, hives, pain, inflammation, bleeding, abnormal collection of blood outside of a blood vessel (haematoma). If this appears to be particularly troublesome, you should discuss this with your doctor.
- Local loss of the fat tissue under the skin, which can be avoided if you change the injection site.
- Carpal tunnel syndrome in adults that is characterised by persistent stinging, burning sensation, pain and/or numbness in the fingers which affect particularly the thumb, index and sometimes also middle and ring finger.

- Fluid retention: peripheral oedema (swelling), muscle pain, numbness and tingling, joint pain, and joint disorders in adult users. These side-effects appear usually early in the treatment, are short-lived and depend on the dose.

- (Isolated) headache.

Uncommon side effects:

- Benign intracranial hypertension (increased intracranial pressure around the brain characterised by headache, nausea, vomiting, double vision and other visual symptoms).
- Carpal tunnel syndrome in children that is characterised by persistent stinging, burning sensation, pain and/or numbness in the fingers which affect particularly the thumb, index and sometimes also middle and ring finger.
- Fluid retention: peripheral oedema (swelling), muscle pain, numbness and tingling, joint pain, and joint disorders in children. These side-effects appear usually early in the treatment, are short-lived and depend on the dose.
- Breast enlargement (one or both sides may be affected).

Very rare side effects:

- Slipped capital femoral epiphysis (a hip problem that starts if the growing end of the thigh bone slips from the ball of the hip joint) and avascular necrosis of the femoral head. If your child shows an unexplained limp and hip or knee pain, please contact your doctor or pharmacist.

- Growth hormone treatment may reduce the levels of thyroid hormone. This can be tested by your doctor and if necessary your doctor will prescribe the adequate treatment.

Side effects with an unknown frequency

You (or your child) can experience allergic reactions due to the treatment with Saizen.

You (or your child) can experience increased insulin levels (hyperinsulinism) as muscle, fat, and liver cells do not respond properly to insulin during growth hormone treatment (insulin resistance). This condition can result in high blood sugar levels (hyperglycaemia). Rarely an inflammation of the pancreas has been reported in patients treated with growth hormone. Leukaemia has been reported in a small number of growth hormone deficiency patients, some of whom have been treated with somatotropin. However, there is no evidence that leukaemia incidence is increased in growth hormone recipients without predisposing factors.

Very rarely a patient could develop antibodies (type of protein that helps protect the body) to somatotropin. These are usually not associated with any side effects and do not usually interfere with growth.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist. This includes any possible 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 or search for MHRA Yellow Card in the Google Play or Apple App Store

Ireland:

HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2

Tel:+353 1 6764971

Fax:+353 1 6762517

Website:www.hpra.ie

e-mail:medsafety@hpra.ie

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Saizen

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

Do not use Saizen after the expiry date which is stated on the cartridge after EXP. The expiry date refers to the last day of that month.

Store the unused Saizen cartridge in a refrigerator (2°C-8°C) in the original package to protect from light. Do not freeze.

After first injection, use within 28 days.

After first injection, the Saizen cartridge, the easypod auto-injector containing the Saizen cartridge or the aluetta pen injector containing the Saizen cartridge has to be stored in a refrigerator (2°C-8°C) for a maximum of 28 days, of which up to 7 days can be outside of a refrigerator at or below 25°C.

When stored outside of the refrigerator for up to 7 days, the Saizen cartridge must be returned to the refrigerator and used within 28 days after first injection.

When using the easypod auto-injector or the aluetta pen injector, the cartridge is kept in the device. The cool.click needle-free auto-injector should be stored outside of a refrigerator always separately from the Saizen cartridge. Protect the used cartridge from light.

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

6. Contents of the pack and other information

What Saizen contains

The active substance is somatotropin (recombinant human growth hormone).

The other ingredients are sucrose, poloxamer 188, phenol, citric acid (for pH adjustment), sodium hydroxide (for pH adjustment), water for injection.

What Saizen looks like and contents of the pack

Saizen 8 mg/ml is a clear to slightly opalescent solution for injection in a pre-filled cartridge (type 1 glass) with a plunger stopper (rubber) and a crimp cap (aluminium and rubber). Pack sizes of 1 and 5 cartridges containing 1.50 ml solution (12 mg somatotropin) or 2.50 ml solution (20 mg somatotropin).

Not all pack sizes may be marketed.

Marketing Authorization Holder

UK: Merck Serono Limited, Bedfont Cross, Stanwell Road, Feltham, Middlesex, TW14 8NX, UK.

IE: Merck Serono (Ireland) Limited, 4045 Kingswood Road, Citywest Business Campus, Dublin, D24 V06K, Ireland.

Manufacturer

Merck Serono SpA, Modugno, Bari, Italy

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