PART III: CONSUMER INFORMATION

PrSaizen® 8.8 mg (5.83 mg/mL) click.easy
(Somatropin for injection)

This leaflet is Part III of a three-part “Product Monograph” published when the drug is approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about SAIZEN. Contact your health care professional if you have any questions about the drug.

ABOUT THIS MEDICATION

What is SAIZEN?
SAIZEN contains somatropin which is identical to growth hormone found naturally in humans but is made in laboratories.

What is SAIZEN used for?
SAIZEN is indicated for:
- the long term treatment of patients with growth failure due to inadequate secretion of growth hormone.
- the treatment of short stature in girls with gonadal dysgenesis (Turner's syndrome) when epiphyses are not closed.
- the treatment of growth failure in children due to Chronic Renal Failure.
- growth disturbance (current height Standard Deviation Score (SDS) < -2) in short children born small for gestational age (SGA) with a birth weight and/or length below -2 standard deviations (SD), who failed to show catch-up growth (Height Velocity SDS < 0 during the last year) by 2 years of age or later.
- replacement therapy in adult patients with acquired or idiopathic growth hormone deficiency (GHD) as diagnosed by a single dynamic test for growth hormone deficiency (peak GH ≤ 5 μg/L).

How SAIZEN works
SAIZEN provides an external supply of human growth hormone for those patients lacking the ability to produce adequate amounts naturally. SAIZEN has many effects on growth and metabolism in patients undergoing therapy;
- stimulates linear growth (growth rate)
- measurable increase in growth (body length) from effects on cartilaginous growth areas of the long bones.
- cellular growth as demonstrated by an increase in the muscular, visceral and red cell mass
- effect on carbohydrate metabolism, including glucose tolerance and insulin levels
- effect on protein metabolism. SAIZEN is an anabolic agent that stimulates intracellular transport of amino acids, net retention of nitrogen and protein synthesis.
- lipid metabolism is also affected when intracellular lipolysis is stimulated, thus increasing the plasma concentration of free fatty acids and stimulating the oxidation of fatty acids.
- connective tissue metabolism is affected by stimulation the synthesis of chondroitin sulfate and collagen as well as the urinary excretion of hydroxyproline
- affects mineral metabolism by inducing the retention of phosphorus and potassium and to a lesser degree sodium.
- also increased are the intestinal absorption of calcium, renal tubular reabsorption of phosphorus with increased serum and inorganic phosphate.

How long is SAIZEN therapy?
Length of time on SAIZEN therapy will vary for every patient. This should be discussed with the patient, parents and doctor throughout the therapy.

Treatment with SAIZEN for growth in children should be discontinued when the patient has reached satisfactory adult height, or the epiphyses (bones) are fused.

When should SAIZEN not be used?
SAIZEN should not be used in the following cases:
- Acute critical illness with complications following cardiac surgery, abdominal surgery, multiple trauma or acute respiratory failure. Clinical studies demonstrated that high doses of another somatropin, were associated with a significantly increased morbidity and mortality in those patients.
- In patients with closed epiphyses, SAIZEN is ineffective for growth. Treatment with SAIZEN should be discontinued when the patient has reached satisfactory adult height, or the epiphyses are fused.
- In the presence of progression of an underlying intracranial tumour. An intracranial tumour should be inactive prior to instituting therapy, and SAIZEN should be discontinued if there is evidence of recurrent activity. Patients should be examined frequently for progression or recurrence of the underlying disease process.
- Patients known to be hypersensitive to somatropin and any of the excipients in powder for solution for injection or the diluent.
- Active neoplasia (either newly diagnosed or recurrent). Any pre-existing neoplasia should be inactive.
- Proliferative or preproliferative diabetic retinopathy.
- In patients with Prader-Willi syndrome who are severely obese or have severe respiratory impairment. Unless patients with Prader-Willi syndrome also have a diagnosis of growth hormone deficiency, SAIZEN is not indicated for long-term treatment of pediatric patients who have growth failure due to genetically confirmed Prader-Will syndrome.

SAIZEN treatment should be discontinued in critically ill patients.

SAIZEN is not recommended for use during pregnancy and lactation.

In children with chronic renal disease, treatment with somatropin must be discontinued at the time of renal transplantation.

The nonmedicinal ingredients of SAIZEN:
Sucrose, phosphoric acid and sodium hydroxide.
**What dosage forms of SAIZEN are available?**

SAIZEN comes as a powder in a vial along with a cartridge of diluent pre-assembled in a reconstitution device (click.easy). SAIZEN 8.8 mg with 1.51 mL of 0.3% metacresol in water for injection. Final concentration that will be injected is 5.83 mg/mL.

Note: SAIZEN is also available in, 3.33 mg and 5 mg, each with vials of diluent, instead of cartridge and without the reconstitution device.

**WARNINGS AND PRECAUTIONS**

- SAIZEN therapy should be carried out under the regular guidance of a doctor who is experienced in the diagnosis and management of patients with growth hormone deficiency.
- Shortly after SAIZEN is given, the patient may feel shaky or light-headed due to low blood sugar levels. The feelings will quickly disappear. The patient’s blood sugar levels may then rise above normal 2-4 hours after administration. Since treatment with growth hormone (GH) can alter how your body handles sugar, the patient’s levels will be tested regularly by a health care professional.
- If the patient is diabetic or a member of the family has diabetes, the doctor will monitor closely the treatment with SAIZEN and may change the treatment for diabetes. The doctor may additionally prescribe another hormone if the patient is found to have developed a lack of thyroid hormone.
- If in the past the patient has had a condition affecting the brain e.g. a tumour, the doctor will examine the patient regularly to check that this has not come back again.
- If the patient suffers from a bad or recurrent headache, or from problems with eyesight and vomiting or feeling sick, contact your doctor immediately. Very rarely, a swelling of the brain may develop and the doctor may want to examine the patient’s eyes to look for any sign of this. In this case it may be necessary to stop the growth hormone treatment, although the treatment may be re-started at a later date. If the symptoms of brain swelling recur, treatment with SAIZEN should be discontinued.
- When the medicine is injected into the same place over a long time, it can cause damage to this area. It is therefore important to keep changing the injection site. The doctor or nurse can speak to you about which parts of the body should be used.
- Some children with growth hormone deficiency have developed leukemia, whether or not they have received treatment with growth hormone, and might be at a slightly higher risk of developing leukemia than non-growth hormone deficient children. No cause and effect relationship with growth hormone treatment have been proven.
- Hip problems may occur more commonly in children with hormone or kidney problems. If the patient 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 the patient develops a limp or complains of hip or knee pain while being treated with SAIZEN, notify your doctor.
- In children with chronic renal failure, treatment should be discontinued at the time of renal transplant.
- Small for Gestational Age (SGA) patients: SGA means small for gestational age. Gestational age is the time a baby is in its mother’s womb. SGA refers to a baby who is smaller than most babies of the same gestational age. Patients who are small for their gestational age have a greater chance of developing diabetes. It is important to have your fasting insulin and blood glucose levels checked before and during treatment with SAIZEN.

**MEDICATION INTERACTION**

It is usually safe to take other medicines. However, if the patient is taking CORTICOSTEROIDS, it is necessary to tell the doctor or nurse. These medicines are used to treat several illnesses including asthma, allergies, kidney rejection and rheumatoid arthritis. These medicines might stop your growth treatment from working. You should tell the doctor or nurse about all medicines that the patient is taking, even those obtained without a doctor’s prescription.

**PROPER USE OF THIS MEDICATION**

**Dosage**

SAIZEN should be injected preferably in the evening.

The dosage and administration schedule of SAIZEN will be adapted to the patient’s body weight by the doctor according to the following scheme:

- **Growth failure due to inadequate endogenous growth hormone secretion:** It is recommended that SAIZEN be administered subcutaneously at a dose of 0.2 mg/kg body weight per week. The dosage can be increased to 0.27 mg/kg per week if there is insufficient response to treatment.
- **Growth failure in girls due to gonadal dysgenesis (Turner’s syndrome):** It is recommended that SAIZEN be administered subcutaneously at a dose of 0.375 mg/kg body weight per week (optimal dosing 0.32 – 0.375 mg/kg/week). Concomitant therapy with non-androgenic anabolic steroids in patients with Turner’s syndrome can enhance the growth response.
- **Growth failure in children with Chronic Renal Failure:** It is recommended that SAIZEN be administered subcutaneously at a dose of 0.35 mg/kg body weight per week.
- **Growth disturbance in short children born small for gestational age (SGA):**
  - It is recommended that SAIZEN be administered subcutaneously at a dose of 0.47 mg/kg body weight/week.
- **Adult Growth Hormone Deficiency:**
  - It is recommended that SAIZEN be administered subcutaneously at a dose of 0.005 mg/kg/day at the start of therapy. This dose may be increased after 4 weeks to 0.01 mg/kg/day if well tolerated. The minimum effective dose should be used and dose requirements may decline with age.

**Preparing SAIZEN for Administration**
The product (powder in vial) must be reconstituted with the bacteriostatic diluent (0.3%(w/v) metacresol in water for injections) provided using the click.easy reconstitution device.

The reconstitution solution is intended for subcutaneous administration (under the skin) and should be clear with no particles. If the solution contains particles, it must not be injected.

Patients should be thoroughly instructed in the reconstitution procedures. For young children, the reconstitution process should be supervised by an adult.

For reconstitution of SAIZEN click.easy please read the following instruction carefully.

- Make sure the click.easy reconstitution device is complete by checking that the SAIZEN vial (a), the sterile transfer cannula (b), and the diluent cartridge (c) are present.
- Check that both the tamper evident seals on the vial container (d) and on the cap (e) are not broken. (picture of tamper evident seal magnified). Do not use the device if the tamper evident seal on the cap is broken, and return it to your pharmacist or doctor.

**How to Reconstitute:**

- Wash your hands with soap and water.
- Find a clean area and lay out the elements needed for the preparation of the medication and the injection

1. Place the click.easy reconstitution device vertically on a flat surface with the vial of powder at the bottom and the cap facing upward.
2. Push firmly on the collar of the base until the vial container is completely inside the main body.
3. Turn the cap clockwise until the green button (f) is visible. You will hear a ‘click’ (Note: the tamper evident seal on the cap is now broken).
4. Holding the click.easy device on a flat surface, push the cap down very slowly and firmly until it will go no further to transfer the diluent from the cartridge into the vial.
5. Check that all the diluent has been transferred into the vial. Dissolve the powder with the diluent by gently swirling the click.easy (Note: A fast transfer of the diluent or shaking will create more foam). Let the solution stand for 2-5 minutes until the powder is completely dissolved.
6. Turn the click.easy upside down and pull the cap slowly downwards until the solution is completely drawn back into the cartridge. Check that no more than one or two drops of solution remain in the vial. If there are more than one or two drops of solution remaining in the vial, slowly push the cap up until some of the solution is back in the vial and gently tap the click.easy. Then draw the solution slowly again back into the cartridge. Remove any excess air that has been drawn into the cartridge by pushing slowly the cap up until no air is visible in the cartridge.
(Note: Avoid pulling the cap down too fast, as this will draw air into the cartridge).

7. Turn the click.easy device sideways with fingers pushing on the cartridge grips, unscrew the cap all the way until it falls off (do NOT pull).

Important: Pulling off the cap (instead of unscrewing it) may break the device & waste the medication.

8. Remove the cartridge containing the reconstituted solution for injection from the click.easy by continuing to hold it on its side, release the cartridge grips and gently pull the end of the cartridge out of the blue plastic container.

9. Carefully peel off the outer label using the tab provided. Write the reconstitution date on the inner label for your records.

10. Discard the click.easy safely in accordance with your local requirements. The cartridge containing the reconstituted solution of SAIZEN is now ready to be used with the one.click™ auto-injector, or easypod™ electromechanical auto-injector.

NOTE: For instructions on how to load the cartridge into the one.click™ auto-injector and inject the reconstituted solution of SAIZEN please read the instructions that have been provided at the end of this leaflet.

For instructions on how to load the cartridge into the easypod™ electromechanical auto-injector, please carefully read the corresponding instruction manual provided with the device.

NOTE: Injections should be given in different parts of your body. Do not use any areas in which you feel lumps, firm knots, depressions, or pain; talk to your doctor or health care professional about anything you find. Clean the skin at the injection site with soap and water.

NOTE: Although SAIZEN in the click.easy device is intended for the one.click™ auto-injector, SAIZEN, once reconstituted, can also be accessed with a conventional syringe for a subcutaneous injection.

What if a Dose is Missed or too Much is Taken?
If a dose is missed or too much SAIZEN injected it is important to 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 the patient will feel shaky and light-headed. If this happens contact your doctor as soon as possible. If too much were taken over a period in time, this could cause an excessive growth of some bones to occur, particularly the hands, feet and jaw.

There have been no reports of the effects of acute overdose.

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

As with any medicine, side effects can sometimes occur, however most people have no problems with their prescribed SAIZEN. Sometimes, however, redness and itching may appear at the injection site. If this appears to be particularly troublesome, you should discuss this with your doctor.

SAIZEN may bring about insulin resistance. Insulin resistance means your body cannot make good use of the insulin it produces. This causes higher levels of glucose in your blood. Your doctor will need to check your blood glucose on a regular basis. It is also important to check blood glucose if you have diabetes or a family history of diabetes.

Intracranial hypertension is pressure within the skull that is too high. This may be a complication of SAIZEN (growth hormone therapy). Call your doctor if you have a headache that does not go away or goes away and comes back, problems with your vision, a sick feeling in your stomach (nausea) or vomiting.

Very rarely a patient could develop antibodies to somatropin. These are usually not associated with any side effects and do not usually interfere with growth.

If the patient shows an unexplained limp, please contact your doctor or nurse.

If the patient suffers from these or any other unwanted effects, please inform your doctor or nurse.

This is not a complete list of side effects. If the patient experiences any unusual symptoms or side effects, you should report them to...
the doctor immediately. It is also wise to discuss the possibility of side effects with the doctor before beginning treatment.

**HOW TO STORE SAIZEN CLICK.EASY**

Unopened vials of SAIZEN are stable for 3 years from the time of manufacture.

Vials of SAIZEN pre-assembled in the click.easy reconstitution device should be stored in the original package at room temperature (25 °C or below).

SAIZEN 8.8 mg (5.83 mg/mL) click.easy should be stored at 2 °C to 8°C in the cartridge and should be used within 28 days.

Do not freeze.

It is important not to use the medicine:
- after the date shown on the vial label
- in case of apparent deterioration.

Keep out of reach of children.

**REPORTING SIDE EFFECTS**

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

**3 ways to report:**
- Online at MedEffect;
- By calling 1-866-234-2345 (toll-free);

By completing a Consumer Side Effect Reporting Form and sending it by:
- Fax to 1-866-678-6789 (toll-free), or
- Mail to: Canada Vigilance Program
  Health Canada, Postal Locator 0701E
  Ottawa, ON
  K1A 0K9
Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

SAIZEN 8.8 mg (5.83 mg/mL) click.easy cartridges can be used with the one.click™ auto-injector or the easypod™ auto-injector. If easypod™ instructions are required, please contact the Growth Support Program at 1-877-724-9361.

**INSTRUCTIONS FOR LOADING THE ONE.CLICK™ AUTOINJECTOR**

**Clicks** | **micro litre (µL)** | **milligam (mg) SAIZEN**
---|---|---
1 | 20 | 0.12
2 | 40 | 0.23
3 | 60 | 0.35
4 | 80 | 0.46
5 | 100 | 0.58
6 | 120 | 0.70
7 | 140 | 0.82
8 | 160 | 0.93
9 | 180 | 1.05
10 | 200 | 1.16
11 | 220 | 1.28
12 | 240 | 1.40
13 | 260 | 1.51
14 | 280 | 1.63
15 | 300 | 1.75
16 | 320 | 1.86
17 | 340 | 1.98
18 | 360 | 2.10
19 | 380 | 2.21
20 | 400 | 2.33
21 | 420 | 2.45
22 | 440 | 2.56
23 | 460 | 2.68
24 | 480 | 2.80
25 | 500 | 2.91
26 | 520 | 3.03
27 | 540 | 3.15
28 | 560 | 3.26
29 | 580 | 3.38

**IMPORTANT INFORMATION**

EMD Serono’s one.click™ auto-injector is to be used exclusively with EMD Serono’s recombinant human growth hormone SAIZEN click.easy in accordance with your medical practitioner’s prescription.

The one.click™ inserts the needle automatically and accurately to the desired depth in the fatty tissue under the skin and administers a pre-selected dose of SAIZEN click.easy with just one click.

Single use disposable sterile needles for the one.click™ are supplied separately. Use only one.click™ needle 0.33 x 12mm - (29G x ½”) distributed by EMD Serono.

The one.click™ containing the cartridge of reconstituted SAIZEN click.easy placed in its storage box should be stored at 2-8°C/36-46°F (refrigerator).

For young children, the injection process should be supervised by an adult.

**I. INSTALLING / CHANGING THE CARTRIDGE**

1. Unscrew and remove the blue activation cap.
2. Unscrew the cartridge cover.

3. Unscrew the cartridge holder. Ensure that the plunger rod comes back inside the main body.

4. Remove the empty cartridge from the cartridge holder, if any. **NOTE:** Clean the empty cartridge holder as recommended in the “CARE OF YOUR one.click™” section V of this manual.

5. Insert a new cartridge containing the reconstituted SAIZEN click.easy into the clean cartridge holder.

6. Screw the cartridge holder with the cartridge back onto the one.click™ main body.

7. Turn the cartridge holder until the plunger disc is against the cartridge - a slight ratchet sound is heard. **NOTE:** For an accurate dosage it is very important that the plunger disc is properly positioned against the cartridge bung.

8. Screw the cartridge cover back onto the one.click™ main body tightly.

**II. SETTING THE INJECTION DEPTH**

Turn the depth adjuster to the position recommended by your medical practitioner. The exposed needle length is approximately as follows:

<table>
<thead>
<tr>
<th>Setting</th>
<th>Fully closed</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposed needle length</td>
<td>8 mm</td>
<td>6 mm</td>
<td>4 mm</td>
<td>2 mm</td>
</tr>
</tbody>
</table>

**III. INJECTION WITH ONE.CLICK™:**

You are now ready to carry out your injection by following the simple steps below:

1. Take a new needle and remove the protective sterility seal. **CAUTION:** Do not use the needle if the sterility seal is damaged or unstuck.

2. Screw the new needle onto the cartridge holder and remove the outer needle cover. Do not remove the inner needle cover.

3. Place the colour end of the blue activation cap on a flat, non-slippery surface.

4. Grip the one.click™ on the cartridge cover and press down until a click is heard. **CAUTION:** Do not press the yellow one.click™ button while activating.

5. Remove the blue activation cap. It will automatically remove the blue inner needle cover.

6. Remove the blue inner needle cover from the blue activation cap by placing its clear end on a flat surface. Press down. The blue inner needle cover pops out.

7. Confirm the injection depth by turning the depth adjuster to the position recommended by your medical practitioner. The exposed needle length is approximately as follows:

<table>
<thead>
<tr>
<th>Setting</th>
<th>Fully closed</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposed needle length</td>
<td>8 mm</td>
<td>6 mm</td>
<td>4 mm</td>
<td>2 mm</td>
</tr>
</tbody>
</table>

8. Turn the green dose dial slowly until the required dose appears in the dose indicator window. When setting the dose, each “click” represents 20 µL. The minimum dose for injection is 1 “click” which is equivalent to 20 µL or 0.12 mg of SAIZEN. The maximum dose is 29 “clicks” which is equivalent to 580 µL or 3.38 mg of SAIZEN. **NOTE:** please refer to DOSE ACCURACY TABLE (clicks / µl / mg) for other dose settings.

**NOTE:** Do not hold the windows on the cartridge cover whilst adjusting the dose avoiding potential drug loss.

**CAUTION:** Never use force when adjusting the dose. If you have any problems setting the dose on your one.click™, see “Additional Information” in section IV of this manual.
9. Prepare the injection site according to the instructions given by your medical practitioner. There is no need to pinch the skin at the injection site.

10. Hold the one.click™ directly (right angle) against the skin.

11. Press the yellow one.click™ button for the injection to start. Keep the one.click™ (approximately 10 seconds) in this position until the injection is completed. Ensure that the green dose dial rewinds to zero.

12. Withdraw the one.click™ from the skin. Pull straight up, not on an angle. After the injection, if a drop of blood appears, simply press for a few seconds on the injection site with a medical wipe.

13. Cover the needle with the outer needle cover and unscrew it. CAUTION: Remember to discard the used needle safely, in a suitable container as recommended by your medical practitioner.

14. Push and screw the blue activation cap back into the cartridge cover.

15. Place your one.click™ with the cartridge containing the remaining reconstituted solution of SAIZEN in its storage box and immediately place the box back into the refrigerator (2-8°C/36-46°F) (not into the freezer).

IV. ADDITIONAL INFORMATION

What if the plunger rod does not move back into the main body when unscrewing the cartridge holder?
Push the plunger rod against a flat surface and it will move back inside the main body.

What if the plunger disc is not properly positioned against the cartridge bung?
Verify that the cartridge holder is properly screwed up into the main body. Turn until a slight ratchet sound is heard.

What if the activation fails and the needle remains visible?
Remove the inner needle cover from the activation cap (point 6 of section III). Remove the needle (point 12 of section III). Repeat the activation with a new needle (points 1 to 4 of section III).

What if I cannot place the blue activation cap to activate the one.click™?
You should check if an old inner needle cover has been left in the blue activation cap.

What if I forget to insert the needle?
You will not be able to activate the one.click™ nor to dial a dose.

What if I cannot set a dose?
Verify if the cartridge is empty. If so, follow instruction of section I “Installing/Changing the cartridge” of this manual.

What if I have gone too far in dialling the dose?
Turn the green dose dial backward to correct the dose.

What if the green dose button turns freely?
If the green dose dial turns freely with no clicking, the one.click™ is probably not activated. Repeat the activation step (point 3,4,5 of section III) ensuring that the blue activation cap is pushed down far enough into the one.click™ or that the cartridge cover is screwed on completely.

What if I cannot dial my complete dosage?
If you cannot dial your dose, you should inject the indicated dose and then complete the injection with a new cartridge.

For example: If you reach a dose value of 14 clicks in the window instead of the desired 20 clicks. You should inject the 14 clicks. Then you should change the cartridge, and change the needle, and set your next dose to 6 clicks (20 minus 14) and inject this amount. This will allow you to have the correct dose and not waste any product.

CAUTION: Never force the dose dial if you do not obtain the required dosing amount.

NOTE: When replacing the cartridge, you may notice small amount of SAIZEN left in the cartridge. This residual amount following the correct use of your one.click™ is normal and cannot be retrieved by the one.click™. Never force the green dose dial trying to recover this leftover SAIZEN as it may lead to the breakage of the one.click™.

What if the green dose dial does not come back to zero?
Replace the cartridge and the needle in the one.click™ with new ones. Notify your medical practitioner, nurse or pharmacist. If the issue is persistent, please send back the one.click™,the cartridge and the needle to your medical practitioner, nurse or pharmacist for replacement.

How do I remove the blue inner needle cover from the activation cap?
According to the one.click™ instruction for use (chapter III, point 6), the blue inner needle cover can be removed by pressing the blue activation cap firmly down against a table.

What if the needle is stuck in the one.click™ and I cannot remove it?
When the one.click™ is activated, the needle is hidden. To remove a stuck needle, you need to remove the cartridge cover. Once the cartridge cover is removed you can safely remove the needle by putting the outer cover on and unscrewing it.
What if the cartridge cover becomes loose?
Unscrew completely the cartridge cover. Secure the cartridge holder by turning clockwise until the plunger disc is against the cartridge bung, you will hear a slight ratchet sound, before screwing again the cartridge cover.

V. GENERAL INSTRUCTIONS
Care of your one.click™:
1. Clean the one.click™ parts with a damp cloth.
2. Clean the cartridge holder of your one.click™ whenever required, or each time you change cartridges. Simply soak the empty cartridge holder in lukewarm water for a few minutes and let it dry in a vertical position.
   **CAUTION:** Soap or any organic solvent should not be used. Never rinse under water or immerse any part of the one.click™ except the cartridge holder.
3. The activation cap will contain small blue particles coming from the removal of the blue inner needle cover. These particles can be removed by tapping the activation cap upside down on a table.
4. If your one.click™ contains a cartridge of reconstituted SAIZEN click.easy it should not be exposed to light or freezing.

TRANSPORTING YOUR ONE.CLICK™
Even for short travel distances, your one.click™ auto-injector containing a cartridge of reconstituted SAIZEN click.easy placed in its storage box should be transported in a cooling bag in order to maintain a temperature of 2-8°C/36-46°F. You should consult your medical practitioner before travelling long distances.

VI. GUARANTEE
Every effort has been made to ensure that the one.click™ will function correctly for at least two years. After two years of operation your one.click™ should be replaced. A new one.click™ auto-injector can be obtained through your medical practitioner, nurse or pharmacist.

Date of receipt of my one.click™:

_____ / _____ / ______
Day     Month     Year

Detailed information on EMD Serono’s SAIZEN click.easy is provided in the respective package leaflet of the drug product.

CE 0086

If you are experiencing any problems with your one.click™, please contact your medical practitioner, nurse or pharmacist or your local EMD Serono representative

pct-199 072

MORE INFORMATION
This document plus the full Product Monograph, prepared for health care professionals can be obtained from

EMD Serono, a subsidiary of EMD Inc., Canada
2695 North Sheridan Way, Suite 200
Mississauga, Ontario, Canada
L5K 2N6

Growth Support Program: 1-877-724-9361

This leaflet was prepared by EMD Serono, a business of Merck KGaA, Darmstadt, Germany.

Last Revised:
PART III: CONSUMER INFORMATION

PrSaizen® 6 mg (5.83 mg/mL), 12 mg (8 mg/mL), 20 mg (8 mg/mL) cartridges
(Somatropin, Solution for injection in a cartridge)

This leaflet is Part III of a three-part “Product Monograph” published when the drug is approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about SAIZEN. Contact your health care professional if you have any questions about the drug.

ABOUT THIS MEDICATION

What is SAIZEN?

SAIZEN contains somatropin which is identical to growth hormone found naturally in humans but is made in laboratories.

What is SAIZEN used for?

SAIZEN is indicated for
- the long term treatment of patients with growth failure due to inadequate secretion of growth hormone.
- the treatment of short stature in girls with gonadal dysgenesis (Turner's syndrome) when epiphyses are not closed.
- the treatment of growth failure in children due to Chronic Renal Failure.
- growth disturbance (current height Standard Deviation Score (SDS) < -2) in short children born small for gestational age (SGA) with a birth weight and/or length below -2 standard deviations (SD), who failed to show catch-up growth (Height Velocity SDS < 0 during the last year) by 2 years of age or later.
- replacement therapy in adult patients with acquired or idiopathic growth hormone deficiency (GHD) as diagnosed by a single dynamic test for growth hormone deficiency (peak GH ≤ 5 μg/L).

How SAIZEN works

SAIZEN provides an external supply of human growth hormone for those patients lacking the ability to produce adequate amounts naturally. SAIZEN has many effects on growth and metabolism in patients undergoing therapy;
- stimulates linear growth (growth rate)
- measurable increase in growth (body length) from effects on cartilaginous growth areas of the long bones.
- cellular growth as demonstrated by an increase in the muscular, visceral and red cell mass
- effect on carbohydrate metabolism, including glucose tolerance and insulin levels
- effect on protein metabolism. SAIZEN is an anabolic agent that stimulates intracellular transport of amino acids, net retention of nitrogen and protein synthesis.
- lipid metabolism is also affected when intracellular lipolysis is stimulated, thus increasing the plasma concentration of free fatty acids and stimulating the oxidation of fatty acids.
- connective tissue metabolism is affected by stimulation the synthesis of chondroitin sulfate and collagen as well as the urinary excretion of hydroxyproline
- affects mineral metabolism by inducing the retention of phosphorus and potassium and to a lesser degree sodium.
- also increased are the intestinal absorption of calcium, renal tubular reabsorption of phosphorus with increased serum and inorganic phosphate.

How long is SAIZEN therapy?

Length of time on SAIZEN therapy will vary for every patient. This should be discussed with the patient, parents and doctor throughout the therapy.

Treatment with SAIZEN for growth in children should be discontinued when the patient has reached satisfactory adult height, or the epiphyses (bones) are fused.

When should SAIZEN not be used?

SAIZEN should not be used in the following cases:
- Acute critical illness with complications following cardiac surgery, abdominal surgery, multiple trauma or acute respiratory failure. Clinical studies demonstrated that high doses of another somatropin, were associated with a significantly increased morbidity and mortality in those patients.
- In patients with closed epiphyses, SAIZEN is ineffective for growth. Treatment with SAIZEN should be discontinued when the patient has reached satisfactory adult height, or the epiphyses are fused.
- In the presence of progression of an underlying intracranial tumour. An intracranial tumour should be inactive prior to instituting therapy, and SAIZEN should be discontinued if there is evidence of recurrent activity. Patients should be examined frequently for progression or recurrence of the underlying disease process.
- Patients known to be hypersensitive to somatropin and any of the excipients in powder for solution for injection or the diluent.
- Active neoplasia (either newly diagnosed or recurrent). Any pre-existing neoplasm should be inactive.
- Proliferative or preproliferative diabetic retinopathy.
- In patients with Prader-Willi syndrome who are severely obese or have severe respiratory impairment. Unless patients with Prader-Willi syndrome also have a diagnosis of growth hormone deficiency, SAIZEN is not indicated for long-term treatment of pediatric patients who have growth failure due to genetically confirmed Prader-Will syndrome.

SAIZEN treatment should be discontinued in critically ill patients.

SAIZEN is not recommended for use during pregnancy and lactation.

In children with chronic renal disease, treatment with somatropin must be discontinued at the time of renal transplantation.

The nonmedicinal ingredients of SAIZEN:
Sucrose, Poloxamer 188, phenol and citric acid.
What dosage forms of SAIZEN are available?

SAIZEN comes as a pre-filled cartridge. There are three presentations which are available:

1. SAIZEN 6 mg with a nominal volume of 1.03 mL of solution. Final concentration that will be injected is 5.83 mg/mL.
2. SAIZEN 12 mg with a nominal volume of 1.50 mL of solution. Final concentration that will be injected is 8 mg/mL.
3. SAIZEN 20 mg with a nominal volume of 2.50 mL of solution. Final concentration that will be injected is 8 mg/mL.

WARNINGS AND PRECAUTIONS

- SAIZEN therapy should be carried out under the regular guidance of a doctor who is experienced in the diagnosis and management of patients with growth hormone deficiency.
- Shortly after SAIZEN is given, the patient may feel shaky or light-headed due to low blood sugar levels. The feelings will quickly disappear. The patient’s blood sugar levels may then rise above normal 2-4 hours after administration. Since treatment with growth hormone (GH) can alter how your body handles sugar, the patient’s levels will be tested regularly by a health care professional.
- If the patient is diabetic or a member of the family has diabetes, the doctor will monitor closely the treatment with SAIZEN and may change the treatment for diabetes. The doctor may additionally prescribe another hormone if the patient is found to have developed a lack of thyroid hormone.
- If in the past the patient has had a condition affecting the brain e.g. a tumour, the doctor will examine the patient regularly to check that this has not come back again.
- If the patient suffers from a bad or recurrent headache, or from problems with eyesight and vomiting or feeling sick, contact your doctor immediately. Very rarely, a swelling of the brain may develop and the doctor may want to examine the patient’s eyes to look for any sign of this. In this case it may be necessary to stop the growth hormone treatment, although the treatment may be re-started at a later date. If the symptoms of brain swelling recur, treatment with SAIZEN should be discontinued.
- When the medicine is injected into the same place over a long time, it can cause damage to this area. It is therefore important to keep changing the injection site. The doctor or nurse can speak to you about which parts of the body should be used.
- Some children with growth hormone deficiency have developed leukemia, whether or not they have received treatment with growth hormone, and might be at a slightly higher risk of developing leukemia than non-growth hormone deficient children. No cause and effect relationship with growth hormone treatment have been proven.
- Hip problems may occur more commonly in children with hormone or kidney problems. If the patient 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 the patient develops a limp or complains of hip or knee pain while being treated with SAIZEN, notify your doctor.
- In children with chronic renal failure, treatment should be discontinued at the time of renal transplant.
- Small for Gestational Age (SGA) patients: SGA means small for gestational age. Gestational age is the time a baby is in its mother’s womb. SGA refers to a baby who is smaller than most babies of the same gestational age. Patients who are small for their gestational age have a greater chance of developing diabetes. It is important to have your fasting insulin and blood glucose levels checked before and during treatment with SAIZEN.

MEDICATION INTERACTION

It is usually safe to take other medicines. However, if the patient is taking CORTICOSTEROIDS, it is necessary to tell the doctor or nurse. These medicines are used to treat several illnesses including asthma, allergies, kidney rejection and rheumatoid arthritis. These medicines might stop your growth treatment from working.

You should tell the doctor or nurse about all medicines that the patient is taking, even those obtained without a doctor’s prescription.

PROPER USE OF THIS MEDICATION

Dosage

SAIZEN should be injected preferably in the evening. The dosage and administration schedule of SAIZEN will be adapted to the patient’s body weight by the doctor according to the following scheme:

- Growth failure due to inadequate endogenous growth hormone secretion: It is recommended that SAIZEN be administered subcutaneously at a dose of 0.2 mg/kg body weight per week. The dosage can be increased to 0.27 mg/kg per week if there is insufficient response to treatment.
- Growth failure in girls due to gonadal dysgenesis (Turner’s syndrome): It is recommended that SAIZEN be administered subcutaneously at a dose of 0.375 mg/kg body weight per week (optimal dosing 0.32 – 0.375 mg/kg/week). Concomitant therapy with non-androgenic anabolic steroids in patients with Turner’s syndrome can enhance the growth response.
- Growth failure in children with Chronic Renal Failure: It is recommended that SAIZEN be administered subcutaneously at a dose of 0.35 mg/kg body weight per week.
- Growth disturbance in short children born small for gestational age (SGA): It is recommended that SAIZEN be administered subcutaneously at a dose of 0.47 mg/kg body weight/week.
- Adult Growth Hormone Deficiency: It is recommended that SAIZEN be administered subcutaneously at a dose of 0.005 mg/kg/day at the start of therapy. This dose may be increased after 4 weeks to 0.01 mg/kg/day if well tolerated. The minimum effective dose should be used and dose requirements may decline with age.

Preparing SAIZEN for Administration

SAIZEN 6 mg (5.83 mg/mL), 12 mg (8 mg/mL), 20 mg (8 mg/mL) cartridges
Place all elements needed for the injection of the medication on a clean surface and wash your hands with soap and water. The cartridge containing the medication of SAIZEN is ready to be used for administration with the easypod™ electromechanical auto-injector. The solution should be clear to slightly opalescent with no particles. If the solution contains particles, it must not be injected.

For instructions on how to load the cartridge into the easypod™ electromechanical auto-injector, please carefully read the corresponding instruction manual provided with the device.

**Picking an Injection Site**

You should pick a different site to inject each day, rotating through arms, legs and abdomen. The buttocks can be used, as well (see Injection Site Diagram). Using a site too often can lead to infection or irritation.

**Injection Site Diagram**

What if a Dose is Missed or too Much is Taken?

If a dose is missed or too much SAIZEN injected it is important to 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 the patient will feel shaky and light-headed. If this happens contact your doctor as soon as possible. If too much were taken over a period in time, this could cause an excessive growth of some bones to occur, particularly the hands, feet and jaw.

There have been no reports of the effects of acute overdose.

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

**SIDE EFFECTS AND WHAT TO DO ABOUT THEM**

As with any medicine, side effects can sometimes occur, however most people have no problems with their prescribed SAIZEN. Sometimes, however, redness and itching may appear at the injection site. If this appears to be particularly troublesome, you should discuss this with your doctor.

SAIZEN may bring about insulin resistance. Insulin resistance means your body cannot make good use of the insulin it produces. This causes higher levels of glucose in your blood. Your doctor will need to check your blood glucose on a regular basis. It is also important to check blood glucose if you have diabetes or a family history of diabetes.

Intracranial hypertension is pressure within the skull that is too high. This may be a complication of SAIZEN (growth hormone therapy). Call your doctor if you have a headache that does not go away or goes away and comes back, problems with your vision, a sick feeling in your stomach (nausea) or vomiting.

Very rarely a patient could develop antibodies to somatropin. These are usually not associated with any side effects and do not usually interfere with growth.

If the patient shows an unexplained limp, please contact your doctor or nurse.

If the patient suffers from these or any other unwanted effects, please inform your doctor or nurse.

This is not a complete list of side effects. If the patient experiences any unusual symptoms or side effects, you should report them to the doctor immediately. It is also wise to discuss the possibility of side effects with the doctor before beginning treatment.

**HOW TO STORE SAIZEN**

SAIZEN 6 mg (5.83 mg/mL), 12 mg (8 mg/mL), 20 mg (8 mg/mL) cartridges:

Do not use SAIZEN after the expiry date, which is stated on the cartridge.

Store cartridge(s) in a refrigerator (2-8ºC) in the original package.

Do not freeze. Store cartridge(s) in a refrigerator (2-8ºC) in the original package.

When using the easypod™ electromechanical auto-injector, the cartridge is kept in the device and the device must be stored in the refrigerator.

Do not freeze. After first injection, the cartridges must be stored at 2-8°C for a period of up to 28 days, of which no more than 7 days may be outside of the refrigerator at or below 25°C.

Cartridges must be discarded after 28 days, or if the total period outside of the refrigerator exceeds 7 days.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required.

**REPORTING SIDE EFFECTS**
You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at MedEffect;
- By calling 1-866-234-2345 (toll-free);

By completing a Consumer Side Effect Reporting Form and sending it by:

- Fax to 1-866-678-6789 (toll-free), or
- Mail to: Canada Vigilance Program
  Health Canada, Postal Locator 0701E
  Ottawa, ON
  K1A 0K9

Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full Product Monograph, prepared for health care professionals can be obtained from

EMD Serono, a subsidiary of EMD Inc., Canada
2695 North Sheridan Way,
Suite 200
Mississauga, Ontario, Canada
L5K 2N6

Growth Support Program: 1-877-724-9361

This leaflet was prepared by EMD Serono is a business of Merck KGaA, Darmstadt, Germany.

Last Revised: