Dosing and Administration Guide

Indication

GENRYZON™ is indicated for the treatment of children and adolescents from 3 years of age with growth disturbance due to insufficient secretion of growth hormone.[3]

genryzon™
(somatrogon) injection

GENRYZON™—a once-weekly GH designed for ease of use[1,4]

ONCE-WEEKLY administration through a multidose, disposable pen that is prefilled and ready to use, with no reconstitution required[1]

The recommended dose is 0.66 mg/kg of body weight administered once weekly by subcutaneous injection, on the same day each week, at any time of the day.[3]

GENRYZON™ 24 mg solution for injection in a prefilled pen[3]

Contains 24 mg of somatrogon in a 1.2-mL solution that delivers a dose in 0.2-mg increments.[3]

- Maximum dose/injection: **12 mg[3]**

GENRYZON™ 60 mg solution for injection in a prefilled pen[3]

Contains 60 mg of somatrogon in a 1.2-mL solution that delivers a dose in 0.5-mg increments.[3]

- Maximum dose/injection: **30 mg[3]**

Sterile needles are required for administration, but are **not included** with the GENRYZON™ pen. GENRYZON™ can be administered with a needle from 4 mm to 8 mm and 31G or 32G.[3]

Choosing the GENRYZON™ pen for your patient[3#]

Considerations depend on the patient and their prescribed dose.
The below examples can be used to guide your decision.

See the sample dosage guide on pages 12-13 for more information.

Dosage (mg/week)	Select Considerations	Suggested Pen
<12	If using the GENRYZON™ 60-mg pen, some of the medication may expire before the patient is able to use it.*	GENRYZON™ 24 mg
12	Both the GENRYZON™ 24-mg pen and the 60-mg pen require a minimum of one injection for this dosage. The 24-mg pen will provide up to two full doses per pen, while the 60-mg pen will provide up to five full doses per pen.	Can depend on the patient (see considerations)
>12 to 24	The GENRYZON™ 24-mg pen requires a minimum of two injections for this dosage range, while the 60-mg pen requires a minimum of one.	GENRYZON™ 60 mg
>24 to 30	The GENRYZON™ 24-mg pen requires a minimum of three injections for this dosage range, while the 60-mg pen requires a minimum of one.	GENRYZON™ 60 mg
>30 to 60	The GENRYZON™ 24-mg pen requires a minimum of three injections for this dosage range, while the 60-mg pen requires a minimum of two.	GENRYZON™ 60 mg

*If it has been more than 4 weeks (28 days) since the date of first use, the pen must be disposed of even if there is some medicine left. The same pen can be used a maximum of five times during this 28-day period.[3]

#Calculated manually based on different dosing schedules, dosage available, full dose an individual can administer and the remaining dose in the pen.

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Overview

- The day of the weekly administration can be changed if necessary as long as the time between the two doses is at least 3 days[3]
- GENRYZON™ should be given in the abdomen, thighs, buttocks, or upper arms. The site of injection should be rotated weekly at each administration[3]
- If more than one injection is required to deliver a complete dose, each injection should be administered at a different injection site[3]
- Single doses of GENRYZON™ higher than 0.66 mg/kg/week have not been studied[3]
- No dose recommendations can be made for patients with hepatic or renal impairment as GENRYZON™ has not been studied in these patients. The safety and efficacy of GENRYZON™ in neonates, infants, and children less than 3 years of age have not yet been established[3]

Switching to GENRYZON™ from daily GH

- Start GENRYZON™ the day after daily GH is discontinued. Administer GENRYZON™ weekly thereafter[3]

Sample patient scenario

Aditya

If Aditya takes his final dose of daily GH on Tuesday, he can take his first dose of GENRYZON™ on Wednesday, and then continue administering GENRYZON™ once weekly on Wednesdays thereafter.

If your patient misses a dose[3]

- If a dose is missed, GENRYZON™ should be administered as soon as possible within 3 days after the missed dose, then the once-weekly dosing schedule should be resumed on the usual injection day. If more than 3 days have passed, the missed dose should be skipped and the next dose should be administered on the regularly scheduled day. In each case, patients can then resume their regular once-weekly dosing schedule

Interactions with other medications[3]

- No drug-drug interaction studies have been performed
- In patients with adrenocorticotropic hormone deficiency who are receiving concomitant GENRYZON™ and glucocorticoid treatments, glucocorticoid dosing should be carefully adjusted to avoid both an inhibitory effect on growth and uncovering central hypoadrenalism
- In patients with diabetes mellitus requiring drug therapy, the dose of insulin and/or oral/injectable antihyperglycemic agent may require adjustment when GENRYZON™ therapy is initiated
- In patients receiving thyroid medicinal products, treatment with daily GH may unmask previously undiagnosed or subclinical central hypothyroidism. Thyroxine replacement therapy may need to be initiated or adjusted
- In female patients on oral estrogen-containing therapy, a higher dose of GENRYZON™ may be required to achieve the treatment goal
- Cytochrome P450–metabolized products—the clearance of compounds metabolized by CYP3A4 (eg, sex steroids, corticosteroids, anticonvulsants, and ciclosporin) may be increased and could result in lower exposure of these compounds

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Abbreviated instructions for use

Please see full Instructions for Use for detailed steps

- Instruct patients to read the Instructions for Use in full before using their pen

IF SETTING UP THE FIRST USE OF A NEW PEN[3]:

- Turn the dose knob to 1.0 for the 60-mg pen; for the 24-mg pen, set the dose knob to 0.4
- Hold the pen with the needle pointing up. **Tap** the cartridge holder gently to float any air bubbles to the top
- Press the injection button until it cannot go any further and you see "0" in the dose window. If liquid appears at the needle tip, the pen is set up. If liquid has not appeared, repeat first-use steps

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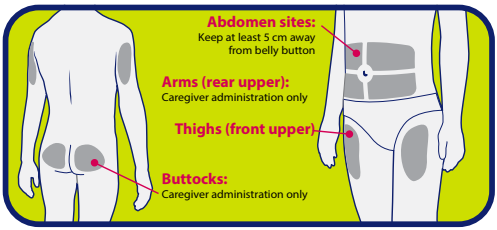
Abbreviated instructions for use (cont)

Getting ready[3]

- Wash and dry your hands
- Use the pen straight from the refrigerator or leave it at room temperature for up to 30 minutes for a more comfortable injection

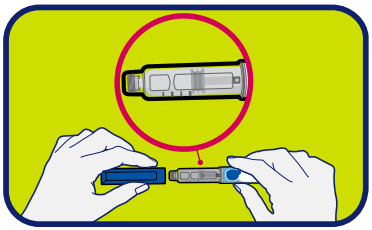
Choose and clean your injection site[3]

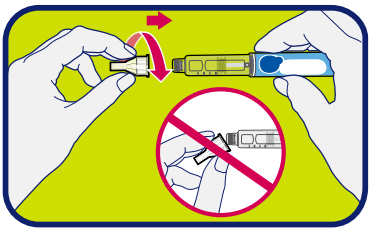
- Injection should be given in the abdomen, front of the upper thighs, buttocks, or back of the upper arms
- Select a different site for each injection
- Do not inject into bony areas; areas that are bruised, red, sore, or hard; and areas that have scars or skin conditions
- Clean the injection site with an alcohol swab and let dry

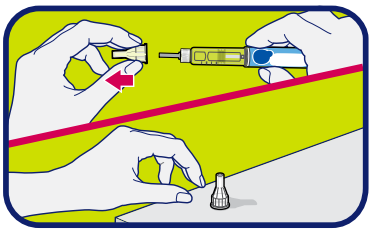


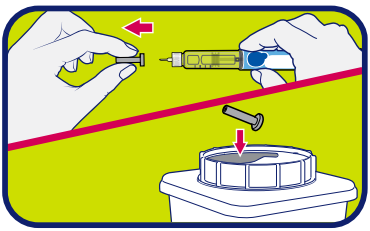
Prepare your injection[3]

- Pull off the pen cap, then set it aside for after the injection. Check that the medicine is colorless to slightly light-yellow and is free of flakes or particles
- Take a new needle and pull off its protective foil. Attach a new needle for each injection
- Pull off the outer needle cover. Set it aside for later to help remove the needle
- Pull off the inner needle cap. Throw away the inner needle cap in a sharps container









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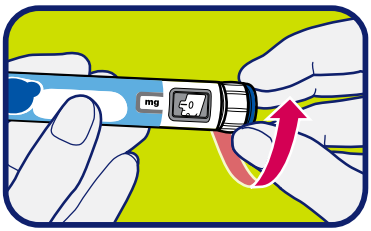
Abbreviated instructions for use (cont)

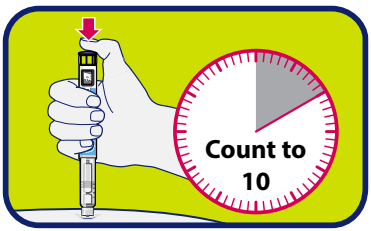
Set your prescribed dose[3]

- Turn the knob to set your dose; dose knob turns 0.5 mg at a time for the GENRYZON™ 60-mg pen and 0.2 mg at a time for the GENRYZON™ 24-mg pen
- **Check the dose window to make sure you have set the correct dose**
- If your dose is more than 30 mg when using the GENRYZON™ 60-mg pen, or more than 12 mg when using the GENRYZON™ 24-mg pen, you will need more than 1 injection. Use a new needle for each injection



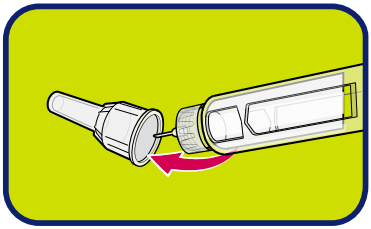
Inject your dose[3]

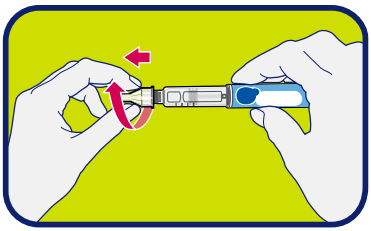
- Hold the pen so you can see the numbers in the dose window
- Insert the needle straight into your skin
- **Press the injection button** until it can't go down any further and "0" is displayed in the dose window. **Hold the button down for 10 seconds,** then let go of the injection button and remove the pen from the injection site by pulling the needle **straight out**

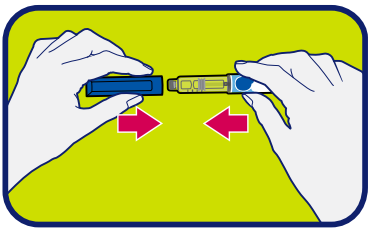


Finish up[3]

- Carefully replace the outer needle cover
- Unscrew the capped needle and dispose of it in a sharps container
- **Do not** reuse needles
- Replace the pen cap. If there is any medicine left, store it in the refrigerator between uses







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Sample dosage guides#

GENRYZON™ 24 mg[3]

Prescribed dosage (mg/week)*	Full doses in one pen†	Remainder in pen after all full doses are used (mg)
5.0	4	4.0
5.2	4	3.2
5.4	4	2.4
5.6	4	1.6
5.8	4	0.8
6.0	4	0
6.2	3	5.4
6.4	3	4.8
6.6	3	4.2
6.8	3	3.6
7.0	3	3.0
7.2	3	2.4
7.4	3	1.8
7.6	3	1.2
7.8	3	0.6
8.0	3	0
8.2	2	7.6
8.4	2	7.2

Prescribed dosage (mg/week)	Full doses in one pen†	Remainder in pen after all full doses are used (mg)
8.6	2	6.8
8.8	2	6.4
9.0	2	6.0
9.2	2	5.6
9.4	2	5.2
9.6	2	4.8
9.8	2	4.4
10.0	2	4.0
10.2	2	3.6
10.4	2	3.2
10.6	2	2.8
10.8	2	2.4
11.0	2	2.0
11.2	2	1.6
11.4	2	1.2
11.6	2	0.8
11.8	2	0.4
12.0	2	0

*For patients who require a dosage of <5 mg/week, they will be able to use the 24-mg pen only four times (for 4 weeks) before it expires and needs to be disposed of.[1]

†If it has been more than 4 weeks (28 days) since the date of first use, the pen must be disposed of even if there is some medicine left. The same pen can be used a maximum of five times during this 28-day period.[1]

‡For patients who require a dosage of ≤12 mg/week, they will be able to use the 60-mg pen only four times (for 4 weeks) before it expires and needs to be disposed of.

#Calculated manually based on different dosing schedules, dosage available, full dose an individual can administer and the remaining dose in the pen.

Adapted from Local Product document GENRYZON LPDGEN092022

GENRYZON™ 60 mg[3]

Prescribed dosage (mg/week)‡	Full doses in one pen†	Remainder in pen after all full doses are used (mg)
12.0	5	0
12.5	4	10.0
13.0	4	8.0
13.5	4	6.0
14.0	4	4.0
14.5	4	2.0
15.0	4	0
15.5	3	13.5
16.0	3	12.0
16.5	3	10.5
17.0	3	9.0
17.5	3	7.5
18.0	3	6.0
18.5	3	4.5
19.0	3	3.0
19.5	3	1.5
20.0	3	0
20.5	2	19.0

Prescribed dosage (mg/week)	Full doses in one pen†	Remainder in pen after all full doses are used (mg)
21.0	2	18.0
21.5	2	17.0
22.0	2	16.0
22.5	2	15.0
23.0	2	14.0
23.5	2	13.0
24.0	2	12.0
24.5	2	11.0
25.0	2	10.0
25.5	2	9.0
26.0	2	8.0
26.5	2	7.0
27.0	2	6.0
27.5	2	5.0
28.0	2	4.0
28.5	2	3.0
29.0	2	2.0
29.5	2	1.0
30.0	2	0

#Calculated manually based on different dosing schedules, dosage available, full dose an individual can administer and the remaining dose in the pen.
Adapted from Local Product document GENRYZON LPDGEN092022

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Storage and disposal

Pen storage

ADVISE PATIENTS TO KEEP GENRYZON™, INJECTION SUPPLIES, AND ALL MEDICINES OUT OF THE REACH OF CHILDREN.[3]

- GENRYZON™ should be stored in a refrigerator at 2°C to 8°C before first use and between each use[3]
- Store GENRYZON™ in the outer carton (or keep the pen cap on) to protect from light. Do not freeze GENRYZON™ or expose GENRYZON™ to heat (above 32°C). Do not use GENRYZON™ if it has been frozen or exposed to heat[3]
- Always remove and safely discard the needle after each injection and store the GENRYZON™ prefilled pen without an injection needle attached[3]
- Always use a new needle for each injection. Replace the cap on your prefilled pen when it is not in use[3]
- The prefilled pen should not be used more than 28 days after first use and should not be used beyond the expiration date. Unused pens may be used until the expiration date printed on the carton, only if the pen has been kept in the refrigerator[3]

Needle and pen disposal[3]

- Any unused product or waste material should be disposed of in accordance with local requirements
- If the prefilled pen is empty, has been used 5 times, or it has been more than 28 days after first use, throw it away even if it contains unused medicine
- A small amount of the sterile GENRYZON™ solution may remain in the pen after all doses have been correctly given. Patients should be instructed not to try to use the remaining solution, but to properly discard the pen

GET GROWING WITH[3]

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References: 1. Deal CL, Steelman J, Vlachopapadopoulou E, *et al*. Efficacy and safety of weekly somatrogon vs. daily somatropin in children with growth hormone deficiency: A phase 3 Study. *J Clin Endocrinol Metab*. 2022;107(7):e2717–e2728. **2.** Zadik Z, Zelinska N, Iotova V, *et al*. An open-label extension of a phase 2 dose-finding study of once-weekly somatrogon vs. once-daily Genotropin in children with short stature due to growth hormone deficiency: Results following 5 years of treatment. *J Pediatr Endocrinol Metab*. 2023;36(3):261–269. Poster 6887 presented at: Annual Meeting of the Endocrine Society [virtual]; March 20-23, 2021. **3.** Adapted from Local Product document GENRYZON LPDGEN092022. **4.** Maniatis AK, Carakushansky M, Galcheva S, *et al*. Treatment burden of weekly somatrogon vs daily somatropin in children with growth hormone deficiency: A randomized study. *J Endocr Soc*. 2022;6(10):bvac117.

genryzon™ (somatrogon) injection

GENRYZON® Summary of Product Information

GENERIC NAME: Somatrogon injection **PRESENTATION:** Somatrogon 24 mg/1.2 ml solution for injection in pre-filled pen and Somatrogon 60 mg/1.2 ml solution for injection in pre-filled pen. **INDICATION(s):** Somatrogon is indicated for the treatment of children and adolescents from 3 years of age with growth disturbance due to insufficient secretion of growth hormone **DOSAGE AND ADMINISTRATION:** The recommended dose is 0.66 mg/kg body weight administered once weekly by subcutaneous injection. Each pre-filled pen is capable of setting and delivering the dose prescribed by the physician. When doses higher than 30 mg are needed (i.e., bodyweight > 45 kg), two injections have to be administered. For patients switching from daily growth hormone medicinal products, the weekly therapy with somatrogon may be initiated at a dose of 0.66 mg/kg/week on the day following their last daily injection. Somatrogon dose may be adjusted as necessary, based on growth velocity, adverse reactions, body weight and serum insulin-like growth factor 1 (IGF-1) concentrations. Somatrogon is administered by subcutaneous injection. Somatrogon is to be injected in the abdomen, thighs, buttocks, or upper arms. The site of injection should be rotated at each administration. Treatment should be discontinued when there is evidence of closure of the epiphyseal growth plates. Treatment should also be discontinued in patients having achieved final height or near final height. The safety and efficacy of somatrogon in patients over the age of 65 years have not been established. Somatrogon has not been studied in patients with renal impairment and hepatic impairment. The safety and efficacy of somatrogon in neonates, infants and children less than 3 years of age have not yet been established. **CONTRAINDICATIONS:** Hypersensitivity to somatrogon or to any of the excipients. Somatrogon must not be used when there is any evidence of activity of a tumour based on experience with daily growth hormone medicinal products. Intracranial tumours must be inactive and antitumour therapy must be completed prior to starting growth hormone (GH) therapy. Treatment should be discontinued if there is evidence of tumour growth. Somatrogon must not be used for growth promotion in children with closed epiphyses. Patients with acute critical illness suffering complications following open heart surgery, abdominal surgery, multiple accidental trauma, acute respiratory failure or similar conditions must not be treated with somatrogon. **WARNING AND PRECAUTIONS:** Hypersensitivity-Serious systemic hypersensitivity reactions (e.g. anaphylaxis, angioedema) have been reported with daily growth hormone medicinal products. **Hypoadrenalism-** Based on published data patients receiving daily growth hormone therapy who have or are at risk for pituitary hormone deficiency(s) may be at risk for reduced serum cortisol levels and/or unmasking of central (secondary) hypoadrenalism. **Thyroid function-** Growth hormone increases the extrathyroidal conversion of T4 to T3 and may unmask incipient hypothyroidism. **Prader-Willi syndrome-** Somatrogon has not been studied in patients with Prader-Willi syndrome. **Glucose metabolism-** Treatment with growth hormone medicinal products may reduce insulin sensitivity and induce hyperglycaemia. **Neoplasm-** In patients with previous malignant disease, special attention should be given to signs and symptoms of relapse. **Benign intracranial hypertension-** Intracranial hypertension (IH) with papilledema, ataxia, visual changes, headache, nausea and/or vomiting has been reported in a small number of patients treated with growth hormone medicinal products. **Acute critical illness-** The benefits of continued somatrogon treatment in this situation should be weighed against the potential risks involved **Pancreatitis-** Although rare in patients treated with growth hormone medicinal products, pancreatitis should be considered in somatrogon-treated patients **Scoliosis-** Because somatrogon increases growth rate, signs of development or progression of scoliosis should be monitored during treatment. **Epiphyseal disorders-** Any paediatric patient with the onset of a limp or complaints of hip or knee pain during treatment should be carefully evaluated. **Oral oestrogen therapy-** If a female patient taking somatrogon begins or discontinues oral oestrogen containing therapy, IGF-1 value should be monitored to determine if the dose of growth hormone should be adjusted to maintain the serum IGF-1 levels within the normal range. **DRUG INTERACTIONS:** No interactions studies in paediatrics have been performed. **Glucocorticoids-** Concomitant treatment with glucocorticoids may inhibit the growth-promoting effects of somatrogon. **Insulin and hypoglycaemic medicinal products-** In patients with diabetes mellitus requiring medicinal product therapy, the dose of insulin and/or oral/injectable hypoglycaemic medicinal products may require adjustment when somatrogon therapy is initiated. **Thyroid medicinal products-** Treatment with daily growth hormone may unmask previously undiagnosed or subclinical central hypothyroidism. **Oral oestrogen therapy-** In female patients on oral oestrogen-containing therapy, a higher dose of somatrogon may be required. Drug-drug interaction studies have not been performed with somatrogon. Somatrogon has been shown to induce CYP3A4 mRNA expression in vitro. The clinical significance of this is unknown. **OVERDOSE:** Single doses of somatrogon higher than 0.66 mg/kg/week have not been studied. Based on experience with daily growth hormone medicinal products, short-term overdose could lead initially to hypoglycaemia and subsequently to hyperglycaemia. Long-term overdose could result in signs and symptoms of gigantism and/or acromegaly consistent with the effects of growth hormone excess. Treatment of overdose with somatrogon should consist of general supportive measures. **ADVERSE REACTION: Very common (≥ 1/10)-** Injection site reactions (injection site pain, erythema, pruritus, swelling, induration, bruising, haemorrhage, warmth, hypertrophy, inflammation, deformation, urticaria), Pyrexia **Common (≥ 1/100 to < 1/10)-** Anaemia, Eosinophilia, Hypothyroidism, Conjunctivitis Allergic, Arthralgia, Pain in extremity. **PHARMACEUTICAL PRECAUTIONS:** Store in a refrigerator (2 °C to 8 °C). Do not freeze. Keep somatrogon in the outer carton to protect from light. **PHARMACOKINETICS / PHARMACODYNAMICS:** Following subcutaneous injection, serum concentrations increased slowly, peaking 6 to 18 hours after dosing. There is no accumulation of somatrogon after once weekly administration. In paediatric patients with GHD, the population PK estimated steady-state peak concentrations following 0.66 mg/kg/week was 636 ng/mL. In paediatric patients with GHD, the population PK estimated apparent central volume of distribution was 0.728 L/kg and apparent peripheral volume of distribution was 0.165 L/kg. The metabolic fate of somatrogon is believed to be classical protein catabolism, with subsequent reclamation of the amino acids and return to the systemic circulation. In paediatric patients with GHD, the population PK estimated apparent clearance was 0.0317 L/h/kg. With a population PK estimated effective half-life of 28.2 hours, somatrogon will be present in the circulation for about 6 days after the last dose.

REFERENCE: Adapted from Local Product document GENRYZON LPDGEN092022

Full prescription information available on request. For the use only of registered medical practitioner, or a hospital or a laboratory

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