PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[PR] SOGROYA®

somapacitan injection

Pre-filled pen for subcutaneous use

5 mg/1.5 mL (3.3 mg/mL),

10 mg/1.5 mL (6.7 mg/mL),

15 mg/1.5 mL (10 mg/mL)

ATC Code: H01AC07

Human Growth Hormone analogue

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RECENT MAJOR LABEL CHANGES

Not Applicable

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Sogroya® (somapacitan injection) is indicated for:

- the long-term treatment of pediatric patients who have growth failure due to an inadequate secretion of endogenous growth hormone (Growth Hormone Deficiency (GHD)).
- the replacement of endogenous growth hormone (GH) in adults with growth hormone deficiency (AGHD).

1.1 Pediatrics

Pediatrics (2.5 years old to epiphyseal fusion): The efficacy and safety of Sogroya® in pediatric patients aged 2.5 years to 11 years with growth failure due to growth hormone deficiency have been established in clinical trials. The efficacy and safety of Sogroya® have not been established in patients under 2.5 years of age. Data on the efficacy and safety of Sogroya® in patients 12 to under 18 years of age are limited. Pediatric patients with a history or presence of malignancy, including intracranial tumours, were not studied in clinical trials [see 14 CLINICAL TRIALS].

1.2 Geriatrics

Elderly patients may be more sensitive to the action of somapacitan, and therefore may be at increased risk for adverse reactions. Initiate Sogroya® with a dose of 1 mg once weekly and use smaller increments when increasing the dose [see 4.2 Recommended dose and Dosage Adjustment].

2 CONTRAINDICATIONS

- Somapacitan must not be used when there is any evidence of neoplastic activity. Intracranial tumours must be inactive and anti-tumour therapy must be completed prior to starting somapacitan therapy. Treatment should be discontinued if there is evidence of tumour growth.
- Somapacitan should not be used for longitudinal growth promotion in children with closed epiphyses.
- Somapacitan is contraindicated in adult patients with acute critical illness suffering from complications following open heart surgery, abdominal surgery, multiple accidental trauma, acute respiratory failure or similar conditions, see 7 WARNINGS AND PRECAUTIONS.
- Somapacitan is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.
- Somapacitan is contraindicated in pediatric patients with Prader-Willi syndrome who are severely obese or have severe respiratory impairment due to risk of sudden death, see 7 WARNINGS AND PRECAUTIONS.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- Sogroya® treatment should be initiated and monitored by physicians who are appropriately qualified and experienced in the diagnosis and management of patients with the condition for which Sogroya® is indicated.
- Sogroya® dosage should be individualized based on the response of each patient (see 4.2 Recommended Dose and Dosage Adjustment).

Switching from other growth hormone products
Switching a patient from another type or brand of growth hormone should be done by a physician who has experience in diagnosis and management in growth hormone deficiency.

Patients switching from daily human growth hormone to once-weekly Sogroya® should choose the preferred day for the weekly dose and stop final dose of daily treatment the day before (or at least 8 hours before) taking the first dose of once-weekly Sogroya®. Patients switching from a weekly human growth hormone to once weekly Sogroya® should continue administration at their once weekly dosing day. Patients should follow the instructions for the dose presented in section 4.2 Recommended Dose and Dosage Adjustment.

4.2 Recommended Dose and Dosage Adjustment

Table 1 - Recommended Doses

Patient population	**Recommended dose**
Pediatric GHD – treatment-naïve or switching from other GH therapy	0.16 mg/kg/week
Adult GHD	**Recommended starting dose**
Aged 18 to <60 years, treatment-naïve or switching from other GH therapy	1.5 mg/week
Aged 60 years or older	1.0 mg/week
Women taking oral estrogens	2.0 mg/week

Pediatric Growth Hormone Deficiency (GHD):

- Initiate Sogroya® with a dosage of 0.16 mg/kg body weight once weekly for treatment-naïve patients and patients switching from daily growth hormone (somatropin), under the supervision of an experienced Healthcare provider.
- Monitor growth rate closely during the first year of Sogroya® treatment. If a patient's growth rate fails to increase in the first year, assess for treatment adherence and other causes of growth failure (e.g. hypothyroidism, undernutrition, advanced bone age).
- Patients who were treated with Sogroya® for GHD in childhood and whose epiphyses are closed should be re-evaluated before continuing Sogroya® according to the Adult posology below.

Treatment evaluation for Pediatric GHD patients

- The dosage of Sogroya® may be decreased from the recommended dose of 0.16 mg/kg/week based on serum IGF-I Standard Deviation Scores (IGF-I SDS) in case of repeated elevations above +2.
- Blood samples for IGF-I SDS sampling may be taken on any day of the week following injections of somapacitan. Sampling 2 days after the injection closely approximates the expected maximum IGF-I value, whereas the average IGF-I concentration over the weekly dosing interval is most closely approximated with a sample taken 4 days after injection (See Table 2 below).

Based on clinical trial data in pediatric GHD patients, a guidance for calculating average IGF-I SDS is provided in Table 2.

Table 2 - Formula for calculating approximate average IGF-I SDS over the weekly dosing interval in pediatric subjects based on blood sampling after injection

Interval **Days (hours) after dose**	**Measured IGF-I SDS adjustment to approximate average IGF-I SDS**
1 day after dose (25-48 hours)	IGF-I SDS – 0.8
2 days after dose (49-72 hours)	IGF-I SDS – 1.0
3 days after dose (73-96 hours)	IGF-I SDS – 0.5
4 days after dose (97-120 hours)	No adjustment*
5 days after dose (121-144 hours)	IGF-I SDS + 0.7
6 days after dose (145-168 hours)	IGF-I SDS + 1.1

* No adjustment based on the result of IGF-I SDS + 0.1, which is considered of negligible clinical relevance

Adult Growth Hormone Deficiency (AGHD):

- Initiate Sogroya® with a dosage of 1.0 to 2.0 mg/week according to Table 1.
- The Sogroya® dose must be individually adjusted for each patient. It is recommended to increase the dose gradually in intervals of 2-4 weeks in steps of 0.5 mg to 1.5 mg based on the patients' clinical response and experience of adverse reactions up to a maximum dose of 8 mg Sogroya® per week.
- The maintenance dose of Sogroya® varies from person to person and between male and female patients. The average Sogroya® maintenance dose in the phase 3 clinical trial was 2.4 mg/week (see 14 CLINICAL TRIALS).

Treatment evaluation for Adult GHD patients

- Serum IGF-I levels (drawn 3-4 days after dosing) can be used as guidance for the dose titration. Dose titration should be individualized, with the aim of reaching IGF-I SDS levels within the age-adjusted upper reference range (IGF-I SDS upper reference range: 0 and +2) within 12 months of titration.
- If this target range cannot be achieved within this period, or the patient does not obtain the desired clinical response, other treatment options should be considered.

- It is recommended that the Sogroya® dose be reduced in patients with repeated IGF-I standard deviation score (SDS) above +2.
- During Sogroya® maintenance treatment, evaluation of efficacy and safety should be considered at approximately 6- to 12-month intervals and may be assessed by evaluating biochemistry (IGF-I-, glucose-, and lipid levels), body composition, and body mass index.

AGHD Patients Aged 60 Years and Older:
Initiate Sogroya® with a dosage of 1 mg once weekly and use smaller dose increments when titrating the dosage. See above for monitoring recommendations and the maximum recommended dosage of Sogroya®.

Patients with Hepatic Impairment
- Sogroya® has not been studied in pediatric patients with hepatic impairment.
- No adjustment of the starting dose is required for adult patients with hepatic impairment. Since the dose of Sogroya® is individually adjusted according to the need of each patient, no additional dose adjustments are required. No information regarding the use of Sogroya®in patients with severe hepatic impairment is available. Sogroya® is not recommended in patients with severe hepatic impairment.

Patients with Renal Impairment
- Sogroya® has not been studied in pediatric patients with renal impairment.
- No adjustment of the starting dose is required for adult patients with renal impairment. Since the dose of Sogroya® is individually adjusted according to the need of each patient, no additional dose adjustments are required.

Gender
Adults: Women may require higher doses of Sogroya® than men. This means that there is a risk that women, especially those on oral estrogen replacement therapy, could be under-dosed. In women using oral estrogen replacement therapy, a change in the route of estrogen administration (e.g. transdermal, vaginal) should be considered. For women on oral estrogen therapy (irrespective of age), initiate Sogroya® with a dosage of 2 mg once weekly.

Race and Ethnicity
Based on population pharmacokinetic/pharmacodynamic analyses, no dose adjustment is required based on race. Ethnicity was not investigated due to small sample size in the development program (15 [4.5%] Hispanic or Latino subjects received somapacitan).

4.4 Administration

Sogroya® is to be administered once weekly at any time of the day.

Patients may self-inject Sogroya® after reading the instructions for use in the Patient Medication Information.

Pediatric GHD patients or their caregivers can inject Sogroya® subcutaneously in the abdomen, thighs, buttocks or upper arms. The injection site should be rotated every week.

Adult GHD patients can inject Sogroya® subcutaneously in the abdomen, thighs or buttocks. The injection site should be rotated every week.

Do not inject into areas where the skin is tender, bruised, erythematous, or indurated.

Flexibility in dosing time:
The day of weekly injection can be changed as long as the time between two doses is at least 4 days (96 hours). After selecting a new dosing day, the once-weekly dosing should be continued.

On occasions when administration at the scheduled dosing day is not possible, once-weekly Sogroya® can be taken up to 2 days before or 3 days after the scheduled weekly dosing day as long as the time between two doses is at least 4 days (96 hours). Regular dosing should be resumed on the scheduled weekly dosing day.

4.5 Missed Dose

Patients who miss a dose are advised to inject Sogroya® upon discovery as soon as possible within 3 days after the missed dose, and then resume their usual once-weekly dosing schedule. If more than 3 days have passed, the dose should be skipped, and the next dose should be administered on the regularly scheduled day. If two or more doses have been missed, the dose should be resumed on the regularly scheduled day.

5 OVERDOSAGE

Sogroya® doses higher than 0.16 mg/kg/week in pediatric patients and 8 mg/week in adult patients have not been studied. Based on experience with daily growth hormone products, short-term overdosage could lead initially to hypoglycemia and subsequently to hyperglycemia. Long-term overdosage could result in signs and symptoms of gigantism and/or acromegaly consistent with the effects of growth hormone excess.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of biologic products, including biosimilars, health professionals should recognize the importance of recording both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Table 3 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Subcutaneous	Solution for injection in a pre-filled pen: 5 mg/1.5 mL 10 mg/1.5 mL	Histidine, Hydrochloric acid (for pH adjustment), Mannitol, Phenol, Poloxamer 188, Sodium hydroxide (for pH adjustment) and Water for Injection

	15 mg/1.5 mL	

The primary packaging for Sogroya® is a 1.5 ml glass cartridge (Type I colourless glass) with a plunger made of chlorobutyl rubber and a stopper made of bromobutyl/isoprene rubber sealed with an aluminium cap.

The cartridge is contained in a multidose disposable colour–coded pen made of polypropylene, polyacetal, polycarbonate and acrylonitrile butadiene styrene and in addition two metal springs. The cartidge is permanently sealed in a pen-injector.

The Sogroya® 5 mg/1.5 mL (3.3 mg/mL) pen delivers doses from 0.025 mg to 2 mg in increments of 0.025 mg (0.0075 mL).

The Sogroya® 10 mg/1.5 mL (6.67 mg/ml) pen delivers doses from 0.05 mg to 4 mg in increments of 0.05 mg (0.0075 mL).

The Sogroya® 15 mg/1.5 mL (10 mg/ml) pen delivers doses from 0.10 mg to 8 mg in increments of 0.1 mg (0.01 mL).

The dose button and cap on the pen-injector is colour–coded according to strength:

- 5 mg/1.5 ml is coloured teal
- 10 mg/1.5 ml is coloured yellow
- 15 mg/1.5 ml is coloured rubine red

Pack size of Sogroya® (5 mg/1.5 ml, 10 mg/1.5 ml and ® 15 mg/1.5 ml) solution for injection in pre-filled pen: a carton containing 1 pen.

7 WARNINGS AND PRECAUTIONS

General

Acute critical illness

Treatment with growth hormone products has been associated with increased mortality in patients with acute critical illness due to complications following open heart surgery, abdominal surgery, or multiple accidental trauma, or those with acute respiratory failure. If patients who are receiving somapacitan become acutely critically ill, discontinue somapacitan (see 2 CONTRAINDICATIONS).

Prader-Willi syndrome

Sogroya® has not been studied in patients with Prader-Willi syndrome. There have been reports of fatalities after initiating therapy with somatropin in pediatric patients with Prader-Willi syndrome who had one or more of the following risk factors: severe obesity, history of upper airway obstruction or sleep apnea, or unidentified respiratory infection.

Carcinogenesis and Mutagenesis

Active malignancy

There is an increased risk of malignancy progression with growth hormone treatment in patients with active malignancy (see 2 CONTRAINDICATIONS). Any pre-existing malignancy should be inactive, and its treatment complete prior to initiating treatment with somapacitan. Discontinue treatment if there is evidence of active malignancy.

Risk of second neoplasm

Based on experience with growth hormone products, there is an increased risk of a second neoplasm (benign and malignant) in childhood cancer survivors. Intracranial tumours, in particular meningiomas in patients treated with radiation to the head for their first neoplasm, were the most common of the second neoplasms. Patients who have achieved complete remission of malignant disease should be followed closely for relapse after commencement of somapacitan treatment.

Risk of malignancy during treatment

There is a risk of malignant changes of pre-existing nevi with growth hormone treatment. Monitor patients on somapacitan therapy carefully for increased growth or potential malignant changes of pre-existing nevi. Advise patients/caregivers to report marked changes in behaviour, onset of headaches, vision disturbances and/or changes in skin pigmentation or changes in the appearance of pre-existing nevi.

Cardiovascular

Edema

Fluid retention during growth hormone replacement may occur. Clinical manifestations of fluid retention (e.g. edema and nerve compression syndromes, including carpal tunnel syndrome) are usually transient and dose dependent.

Endocrine and Metabolism

Adrenocortical insufficiency

Patients receiving growth hormone therapy who have or are at risk for corticotropin deficiency may experience reduced serum cortisol levels and/or unmasking of central (secondary) hypoadrenalism. In addition, patients treated with glucocorticoid replacement for previously diagnosed hypoadrenalism may require an increase in their maintenance or stress doses following initiation of growth hormone treatment. Monitor patients for reduced serum cortisol levels and/or need for glucocorticoid dose increases in those with known hypoadrenalism.

Glucose intolerance and diabetes mellitus

Treatment with growth hormone may decrease insulin sensitivity, particularly at higher doses. As a result, hyperglycemia and new onset type 2 diabetes mellitus have been reported in patients taking growth hormone. Glucose levels should be monitored periodically in all patients treated with growth hormone, especially in those with risk factors for diabetes mellitus. Patients with pre-existing type 1 or type 2 diabetes mellitus or impaired glucose tolerance should be monitored closely during growth hormone therapy (see 9.4 Drug-Drug Interactions). The doses of antidiabetic agents may require adjustment when growth hormone therapy is initiated in these patients.

Thyroid function

Growth hormone increases the extrathyroidal conversion of T4 to T3 and may as such unmask incipient hypothyroidism. As hypothyroidism interferes with the response to growth hormone therapy, patients

should have their thyroid function tested regularly, and should receive replacement therapy with thyroid hormone when indicated.

Gastrointestinal

Pancreatitis

Cases of pancreatitis have been reported in patients receiving growth hormone treatment. The risk may be greater in pediatric patients compared with adults. Consider pancreatitis in patients who develop persistent severe abdominal pain.

Immune

Lipohypertrophy/lipoatrophy

When Sogroya® is administered at the same site over a long period of time, lipohypertrophy or lipoatrophy may occur. The injection site should be rotated to reduce the risk.

Hypersensitivity

Serious systemic hypersensitivity reactions (e.g. anaphylaxis, angioedema) have been reported with growth hormone products. If a serious hypersensitivity reaction occurs, immediately discontinue use of somapacitan and treat promptly per standard of care and monitor until signs and symptoms resolve. Do not use in patients with previous hypersensitivity to somapacitan (see 2 CONTRAINDICATIONS).

Musculoskeletal

Epiphyseal disorders

Epiphyseal disorders, including slipped capital femoral epiphysis, may occur more frequently in patients undergoing rapid growth. Any pediatric patient with the onset of a limp or complaints of hip or knee pain during treatment should be carefully evaluated.

Scoliosis

Growth hormone treatment increases growth rate, and progression of preexisting scoliosis can occur in patients who experience rapid growth. Growth hormone treatment has not been shown to increase the occurrence of scoliosis. Monitor patients with a history of scoliosis for disease progression.

Neurologic

Benign intracranial hypertension

In the event of severe or recurrent headache, visual symptoms, nausea, and/or vomiting, a fundoscopy for papilledema is recommended. If papilledema is confirmed, a diagnosis of benign intracranial hypertension should be considered and growth hormone treatment should be stopped. Once signs and symptoms have resolved, if growth hormone treatment is restarted, consider restarting at a lower dose. Careful monitoring for symptoms of intracranial hypertension is necessary.

Reproductive Health: Female and Male Potential

- **Fertility**

  There is no clinical experience with Sogroya® use and its potential effect on fertility.

  Animal Data

  In an animal fertility study, somapacitan induced irregular estrus cycles and longer estrus cycles in

female rats; however, no adverse effects on fertility were observed (see 16 NON-CLINICAL TOXICOLOGY).

7.1 Special Populations

7.1.1 Pregnant Women

There are no available data on Sogroya® use in pregnant women.

Animal Data (see 16 NON-CLINICAL TOXICOLOGY)

In an embryo-fetal development study in rats, somapacitan administration to pregnant rats during the period of organogenesis resulted in fetal skeletal malformations consisting of short/bent/thickened long bones at a dose of 18 mg/kg body weight/day (305 times the clinical exposure at the maximum recommended human dose [MRHD] of 8 mg/week), which were not observed at lower doses of 2 and 6 mg/kg body weight/day (5 and 24 times the clinical exposure at the MRHD of 8 mg/week).

In an embryo-fetal development study in rabbits, somapacitan administration to pregnant rabbits during the period of organogenesis resulted in reduced fetal growth at doses ≥1 mg/kg body weight every two days (≥ 17 times the clinical exposure at the MRHD of 8 mg/week).

In a pre-and post-natal development study in rats, somapacitan administration to pregnant rats resulted in an increased incidence of renal pelvic dilatation in F1 offspring on post-natal day 21 at doses ≥4mg/kg body weight twice weekly (29 times clinical exposure at the MRHD of 8 mg/week), but which was not observed in the adult F1 generation. Acyclic estrus cycles were also observed in F1 female offspring following maternal dosing at 18 mg/kg body weight twice weekly (787 times the clinical exposure at the MRHD of 8 mg/week). In addition, somapacitan was detected in F1 offspring plasma following maternal exposure at a dose of 18 mg/kg body weight twice weekly.

Somapacitan and/or its metabolites have been detected in rat fetal tissues (highest concentration in fetal kidneys) following administration to pregnant rats, indicating transfer across the placental barrier.

7.1.2 Breast-feeding

There is no information on the presence of Sogroya® in human milk, the effects on the breastfed infant, or the effects on milk production. Somapacitan-related material has been observed to be secreted into milk of lactating rats. When a substance is present in animal milk, it is likely that the substance will be present in human milk. A risk to the breastfed newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Sogroya® therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

7.1.3 Pediatrics

The efficacy and safety of Sogroya® have been evaluated in pediatric patients with growth failure due to growth hormone deficiency (see 1 INDICATIONS).

7.1.4 Geriatrics

In clinical studies a total of 80 (24%) of the 333 Sogroya® treated patients were 60 years or older and 3 (0.9%) were 75 years or older [see 14 CLINICAL TRIALS]. Subjects older than 60 years appeared to have higher exposure than younger subjects at the same dose level. Elderly patients may be more sensitive to the action of somapacitan, and therefore may be at increased risk for adverse reactions. Therefore, lower doses of Sogroya® may be necessary in older patients. For further information, see 4.2 Recommended Dose and Dosage Adjustment.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

In pediatric patients, the most common adverse reactions (ADRs) are (from pivotal trial 4263 (REAL 4) in decreasing order) headache (12%), hypothyroidism (5%), injection site reactions* (5%), peripheral edema (3%), arthralgia (2%), hyperglycemia (2%), fatigue (2%), and adrenocortical insufficiency (1.5%).

In adults, the most common adverse drug reactions (ADRs) are (from pivotal trial 4054 (REAL 1) in decreasing order) headache (12%), arthralgia (7%), fatigue (6%) peripheral oedema (4%), adrenocortical insufficiency (3%), asthenia (3%), paresthesia (2%), hypothyroidism (1.8%), injection site reaction (1%), hyperglycemia (1%), carpal tunnel syndrome (0.9%) and lipohypertrophy (0.4%).

* The injection site reactions were injection site bruising (1.5%), injection site pain (1.5%), injection site hematoma (1.5%) and injection site swelling (0.8%)

8.2 Clinical Trial Adverse Reactions - Pediatrics

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

Sogroya® was studied in a 52-week randomized, multi-national, open label, active-controlled, parallel-group clinical study in 200 treatment naïve, prepuberal pediatric patients with growth hormone deficiency [see 14 CLINICAL TRIALS]. Table 4 shows common adverse events that occurred in >2% of patients treated in this trial.

Table 4 - Adverse Events occurring >2% in Sogroya®-Treated Pediatric Patients and More Frequently than in Daily Somatropin-Treated Pediatric Patients (52 Weeks of Treatment)

	Somatropin (n = 68) %	Sogroya® (n = 132) %
Endocrine Disorders		
Hypothyroidism	1.5	3.0
Gastrointestinal		
Constipation	1.5	3.0
General disorders and administration site conditions		
Swelling face	0	2.3
Musculo-skeletal and connective tissue		
Pain in extremity	2.9	9.1

	Somatropin (n = 68) %	Sogroya® (n = 132) %
Nervous system disorders		
Headache	8.8	12.1
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS		
Cough	2.9	4.5
Infections and infestations		
Nasopharyngitis	10.3	11.4
Respiratory tract infection	2.9	3.0
Upper respiratory tract infection	1.5	2.3

Headache was very commonly observed (12%). Almost all of the cases were of mild severity, and the majority of the cases recovered.

8.2.1 Clinical Trial Adverse Reactions – Adults

Sogroya® was studied in adult patients with GHD in a 35-week, placebo-controlled, double-blind trial with an active-control arm [see 14 CLINICAL TRIALS]. Adverse events occurring >2% with Sogroya® are presented in Table 5.

Table 5 - Adverse Events occurring >2% in Adults with GHD Treated with Sogroya® and More Frequently# than in Placebo-Treated Patients for 34 Weeks

	Sogroya® (n = 120) %	Placebo (n = 61) %
Blood and lymphatic system disorders		
Anemia	2.5	0
Gastrointestinal		
Dyspepsia	5	3.3
Vomiting	3.3	1.6
General disorders and administration site conditions		
Peripheral edema	3.3	1.6
Metabolism and nutrition disorders		
Adrenal insufficiency	3.3	1.6
Musculo-skeletal and connective tissue		
Back Pain	10	3.3
Arthralgia	6.7	1.6
Nervous system disorders		
Dizziness	4.2	1.6
Psychiatric disorders		
Sleep disorder	4.2	1.6
Infections and infestations		
Tonsillitis	3.3	1.6
Investigations		
Blood creatine phosphokinase increase	3.3	0
Weight increased	3.3	0
Vascular disorders		
Hypertension	3.3	1.6

[#] Included adverse reactions reported with at least 1% greater incidence in Sogroya® group compared to the placebo group

More Sogroya® treated patients shifted from normal baseline levels to elevated phosphate and creatine phosphokinase levels at the end of the trial compared to the placebo group (17.5% vs 4.9% and 9.2% vs. 6.6%, respectively); these laboratory changes occurred intermittently, and were non-progressive.

8.3 Less Common Clinical Trial Adverse Reactions - Pediatrics

Clinical trial adverse events with a frequency of less than 2%, and more frequently than somatropin, in patients treated with somapacitan in the pivotal study 4263 (see 14 CLINICAL TRIALS) are presented in the following listing:

Blood and lymphatic system disorders - Lymphadenopathy, Anemia

Congenital, familial and genetic disorders – Cryptorchism

Ear and labyrinth disorders - Cerumen impaction, Tinnitus

Endocrine disorders - Secondary hypothyroidism, Adrenocorticotrophic hormone deficiency, Secondary adrenocortical insufficency

Eye disorders - Eye irritation, Eye pruritus, Eyelid cyst, Hypermetropia, Periorbital edema

Gastrointestinal disorders - Abdominal pain, Gastrooesophageal reflux disease, Toothache, Umbilical hernia

General disorders and administration site conditions - Fatigue, Injection site hematoma, Chest discomfort, Face edema, Hyperthermia, Injection site swelling, Local reaction, Peripheral swelling, Swelling

Immune system disorders - Food allergy

Infections and infestations - Gastroenteritis viral, Hand-foot-and-mouth disease, Otitis media acute, Acute sinusitis, Fungal infection, Gastrointestinal viral infection, Herpangina, Impetigo, Infection, Infection parasitic, Latent tuberculosis, Pharyngitis, Pneumonia, Respiratory tract infection viral, Sinusitis, Streptococcal infection, Tonsillitis streptococcal, Tracheitis, Urinary tract infection, Viral upper respiratory tract infection

Injury, poisoning and procedural complications - Hand fracture, Head injury, Accidental underdose, Concussion, Eye contusion, Fall, Foot fracture, Joint dislocation, Nasal injury, Procedural pain, Skin abrasion, Skin laceration, Venomous sting

Investigations - Low density lipoprotein increased, Blood cholesterol abnormal, Blood creatine phosphokinase increased, Blood glucose increased, Blood thyroid stimulating hormone increased, Cortisol decreased, SARS-CoV-2 test positive

Neoplasms benign, malignant and unspecified (incl cysts and polyps) - Lymphangioma

Nervous system disorders - Cognitive disorder, presyncope, somnolence

Metabolism and nutrition disorders - Dehydration, Dyslipidaemia, Impaired fasting glucose, Iodine deficiency

Musculoskeletal and connective tissue disorders - Myalgia, Arthritis reactive, Growing pains

Psychiatric disorders - Anxiety, Enuresis, Nightmare, Sleep disorder

Reproductive system and breast disorders - Balanoposthitis

Respiratory, thoracic and mediastinal disorders - Upper respiratory tract inflammation, Rhinitis allergic, Adenoidal hypertrophy, Nasal congestion, Rhinorrhoea

Skin and subcutaneous tissue disorders - Dermatitis atopic, Erythema, Pruritus, Alopecia, Dry skin, Henoch-Schonlein purpura, Keratosis pilaris, Lipodystrophy acquired, Miliaria, Poikiloderma, Psoriasis, Skin fissures

8.3.1 Less Common Clinical Trial Adverse Reactions – Adults

Clinical trial adverse events with a frequency of less than 2%, and more frequently than somatropin and placebo, in patients treated with somapacitan in the pivotal study 4054 (see 14 CLINICAL TRIALS) are presented in the following listing:

Blood and lymphatic system disorders - Lymphadenopathy, Iron deficiency anaemia, Thrombocytopenia

Cardiac disorders - Cardiovascular disorder, Cardiac discomfort, Mitral valve incompetence, Aortic valve incompetence, Left ventricular dysfunction

Congenital, familial and genetic disorders - Myotonia congenita

Endocrine disorders - Adrenocortical insufficiency acute, Thyroid mass

Eye disorders - Conjunctival haemorrhage, Eye pruritus, Dry eye

Gastrointestinal disorders - Epigastric discomfort, Dry mouth, Abdominal distension, Inguinal hernia, Large intestine polyp

General disorders and administration site conditions - Non-cardiac chest pain, Nodule

Immune system disorder - Seasonal allergy

Infections and infestations - Herpes zoster, Ear infection, Lower respiratory tract infection, Cystitis, Oral herpes, Pharyngitis streptococcal, Herpes simplex, Otitis media, Vaginal infection, Pilonidal cyst, Tooth abscess, Upper respiratory tract infection bacterial, Laryngitis, Hordeolum, Viral infection, Sepsis

Injury, poisoning and procedural complications - Arthropod sting, Limb injury, Wrist fracture

Investigations - Blood creatinine increased, Blood alkaline phosphatase increased, Blood bilirubin increased, Blood potassium decreased, Thyroxine decreased, Lymph node palpable, Creatinine renal clearance increased, Gamma-glutamyltransferase increased, Electrocardiogram abnormal, Thyroid hormones decreased

Metabolism and nutrition disorders - Gout, Fluid retention, Hypertriglyceridaemia, Hypoglycaemia, Vitamin D deficiency

Musculoskeletal and connective tissue disorders - Muscular weakness, Intervertebral disc degeneration, Costochondritis, Exostosis, Joint effusion, Limb deformity, Intervertebral disc protrusion, Muscle twitching, Myositis, Osteoarthitis, Plantar fasciitis

Nervous system disorders - Hypersomnia, Sciatica

Psychiatric disorders - Emotional disorder, Depression

Renal and urinary disorders - Bladder pain, Polyuria, Urinary incontinence

Reproductive system and breast disorders - Nipple pain

Respiratory, thoracic and mediastinal disorders - Paranasal sinus hypersecretion, Dyspnoea paroxysmal nocturnal, Pharyngeal erythema, sinus congestion, nasal congestion

Skin and subcutaneous tissue disorders - Lipohypertrophy, Lipodystrophy acquired, Onychoclasis, Papule, Acne, Alopecia, Dermatitis allergic, Skin mass, Rash erythematous, Rash papular, hyperkeratosis, rash generalised, pustular psoriasis

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

No formal drug interaction studies have been performed with somapacitan.

9.4 Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table 6 - Clinically important Drug Interactions with Sogroya®

[Proper/Common name]	Source of Evidence	Effect	Clinical Comment
Microsomal enzyme 11β-hydroxysteroid	T	Microsomal enzyme 11β-hydroxysteroid dehydrogenase type 1 (11βHSD-1) is required for conversion of cortisone to its active metabolite, cortisol, in hepatic and adipose tissue. GH inhibits 11βHSD-1. Consequently, individuals with untreated GH	Patients treated with glucocorticoid replacement for hypoadrenalism may require an increase in their maintenance or stress doses following initiation of SOGROYA (see 7 WARNINGS AND PRECAUTION).

		deficiency have relative increases in 11βHSD-1 and serum cortisol. Initiation of Sogroya® may result in inhibition of 11βHSD-1 and reduced serum cortisol concentrations.	
Cytochrome P450-Metabolized Drugs	T	Limited published data indicate that GH treatment increases cytochrome P450 (CP450)-mediated antipyrine clearance. Sogroya® may alter the clearance of compounds known to be metabolized by CP450 liver enzymes.	Careful monitoring is advisable when Sogroya® is administered in combination with drugs metabolized by CP450 liver enzymes.
Oral Estrogen	T	Oral estrogens may reduce the serum IGF-I response to Sogroya®.	Patients receiving oral estrogen replacement may require higher Sogroya® dosages (see 4 DOSAGE AND ADMINISTRATION).
Insulin and/or Other Hypoglycemic Agents	T	Treatment with Sogroya® may decrease insulin sensitivity, particularly at higher doses.	Patients with diabetes mellitus may require adjustment of their doses of insulin and/or other hypoglycemic agents (see 7 WARNINGS AND PRECAUTIONS).

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Somapacitan (as well as endogenous GH) binds to a dimeric GH receptor in the cell membrane of target cells resulting in intracellular signal transduction and a host of pharmacodynamic effects. Some of these pharmacodynamic effects are primarily mediated by IGF-I produced in the liver and also locally (e.g., skeletal growth, protein synthesis), while others are primarily a consequence of the direct effects of somapacitan (e.g., lipolysis).

10.2 Pharmacodynamics

A dose-dependent IGF-I response that is less than dose-proportional is induced following somapacitan administration in AGHD patients (n = 26). Steady state IGF-I was reached after 1-2 weekly doses with

limited cumulative IGF-I concentrations. The IGF-I response is maximal within 2 to 4 days after dosing.

In pediatric GHD patients somapacitan produces a dose linear IGF-I response, with a change of 0.02 mg/kg on average resulting in a change in IGF-I standard deviation score (SDS) of 0.32.

Cardiac electrophysiology (QTc)
The potential effect of somapacitan in adult GHD patients on cardiac repolarisation was assessed based on ECGs collected at around the time of C_{max} for somapacitan at therapeutic doses in the pivotal phase 3 trial REAL 1. There was no correlation/association between the change from baseline in QTcF and the somapacitan concentration. The results of the overall interpretation of ECGs and the evaluation of adverse events related to cardiac safety did not indicate any safety signals.

10.3 Pharmacokinetics

The pharmacokinetics (PK) of somapacitan following subcutaneous administration have been investigated at dose levels from 0.02 to 0.16 mg/kg/week in pediatric GHD patients, at dose levels from 0.02 to 0.12 mg/kg in adult GHD patients, and at dose levels from 0.01 to 0.32 mg/kg in healthy adults.

Overall, somapacitan displays non-linear pharmacokinetics. In the clinically relevant dose range of somapacitan in adults with GHD, somapacitan pharmacokinetics are approximately linear.

Table 7 - Summary of somapacitan pharmacokinetic parameters in pediatric and adult patients during steady-state dosing

	Dose	$AUC_{0\text{-}tau}$ (ng*h/mL)	C_{avg} (ng/mL)	C_{max} (ng/mL)	t_{max} (h)	t1/2 (h)	R_{acc}
GHD	0.16 mg/Kg/week	13500	80.2	299	21.1	33.6	1.06
AGHD	2.4 mg/week	448	2.67	7.42	5.81	69.2	1.23

Abbreviations: $AUC_{0\text{-}tau}$: Average steady-state area under the curve over a dosing interval, C_{avg}: Average steady-state concentration in a dosing interval, C_{max}: Maximum concentration, t1/2: terminal half-life, t_{max}: time of maximum somapacitan concentration, R_{acc}: accumulation ratio at steady state compared to single dose.

Absorption:
In adult and pediatric patients with GHD median t_{max} ranged from 4 to 24 hours at doses from 0.02 mg/kg/week to 0.16 mg/kg/week.

In adult and pediatric patients with GHD, steady state exposure was achieved following 1-2 weekly doses, with little to no accumulation present (mean accumulation ratio < 1.5). The absolute bioavailability of somapacitan in humans has not been investigated.

Distribution:
Somapacitan is extensively bound (>99%) to plasma proteins and is expected to be distributed like albumin.

Based on population PK analyses, the estimated volume of distribution (V/F) was 1.7 L in pediatric GHD patients and 14.6 L in adult GHD patients.

Metabolism:
Somapacitan is extensively metabolised by proteolytic degradation, and cleavage of the linker sequence between the peptide and albumin binder.
In adult GHD patients, somapacitan was extensively metabolised before excretion, and no intact somapacitan was found neither in urine, which was the main excretion route (81%), nor in feces where 13% of somapacitan related material was found, indicating full biotransformation before excretion.

Elimination:
Based on population-PK analysis, the terminal half-life was 34 h in pediatric GHD patients and 69 h in adult GHD patients.

Special Populations and Conditions
It is recommended that the dose is adjusted based on the clinical response and the patient's experience of adverse events. No additional dosing considerations of somapacitan is needed based on race (Japanese, Asian non-Japanese vs White), body weight, renal or hepatic impairment. For starting dose and dose adjustment information, refer to Section 4.2 Recommended Dose and Dosage Adjustment.

- **Pediatrics:** Based on population pharmacokinetic analysis gender, race and body weight do not have a clinically meaningful effect on the pharmacokinetics following weight-based dosing.
- **Geriatrics:** Adult patients greater than 60 years of age and geriatric patients have a higher exposure than younger subjects at the same somapacitan dose [see 4.2 Recommended Dose and Dosage Adjustment].
- **Sex:** Female patients and in particular female patients on oral estrogen replacement, have lower exposure (53% for females on oral estrogen replacement and 30% for females not on oral estrogen replacement) than male subjects at the same somapacitan dose. A higher starting dose for females on oral estrogen replacement is recommended in Section 4.2 Recommended Dose and Dosage Adjustment.
- **Hepatic Insufficiency:** A somapacitan dose of 0.08 mg/kg at steady state resulted in higher exposure in subjects with moderate hepatic impairment with ratios to normal hepatic function of 4.69 for $AUC_{0\text{-}168h}$ and 3.52 for C_{max}.
  Lower somapacitan stimulated IGF-I levels were observed in subjects with mild and moderate hepatic impairment compared to subjects with normal hepatic function (ratio to normal was 0.85 for mild and 0.75 for moderate).
- **Renal Insufficiency:** A somapacitan dose of 0.08 mg/kg at steady state resulted in higher exposures in subjects with renal impairment, most pronounced in subjects with severe renal impairment and in subjects requiring hemodialysis, where $AUC_{0\text{-}168h}$ ratios to normal renal function were 1.75 and 1.63, respectively. In general, somapacitan exposure tended to increase with decreasing GFR.
  Higher IGF-$I_{AUC0\text{-}168h}$ levels were observed in subjects with moderate and severe renal impairment and subjects requiring hemodialysis, with ratios to normal renal function of 1.35, 1.40 and 1.24 respectively.
- **Body weight:** Despite a higher exposure in adult GHD patients with low body weight as compared to subjects with high body weight at the same somapacitan dose, subjects needed similar doses to reach similar IGF-I levels across the body weight range 35 kg to 150 kg. No dose adjustment is required.

11 STORAGE, STABILITY AND DISPOSAL

Before and during use: Store in a refrigerator at 2°C to 8°C with the cap on and in the original carton to protect from light. Do not freeze or store directly adjacent to the refrigerator cooling element. Do not use Sogroya® if it has been frozen. Discard pre-filled pen if kept above 30°C. Avoid direct or excessive heat. Avoid sunlight.

Write the date of first use in the space provided on the carton.

Always remove and safely discard the needle after each injection and store the Sogroya® pre-filled pen without an injection needle attached. Always use a new needle for each injection to prevent contamination.

Table 8 - Storage Options for Sogroya®

Sogroya®	**Before first use (unopened)**		**After first use (opened)**	
	Refrigerated 2°C to 8°C	Room Temperature up to 30°C	Refrigerated 2°C to 8°C	Room Temperature up to 30°
5 mg/1.5 mL	Until expiry date	Maximum 72 hours (3 days)*	Up to 6 weeks	Maximum 72 hours (3 days)*
10 mg/1.5 mL				
15 mg/1.5 mL				

*To allow for portability, the total time allowed at room temperature (up to 30°C) is 72 hours (3 days) regardless of whether the product is in-use (opened) or before first use (unopened). Must be discarded if kept above 30°C.

Needles and other waste material should be disposed of in accordance with local requirements.

12 SPECIAL HANDLING INSTRUCTIONS

The pen is for use by one person only.

Sogroya® should not be used if the solution does not appear clear to slightly opalescent, colourless or slightly yellow and free from visible particles.

The cartridge must not be taken out of the pre-filled pen and refilled.

Sogroya® can be administered with a needle up to a length of 8 mm. The pen is designed to be used with NovoFine® disposable needles. The needles are not included in the carton.

Patients are advised to read these instructions very carefully before using Sogroya®.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

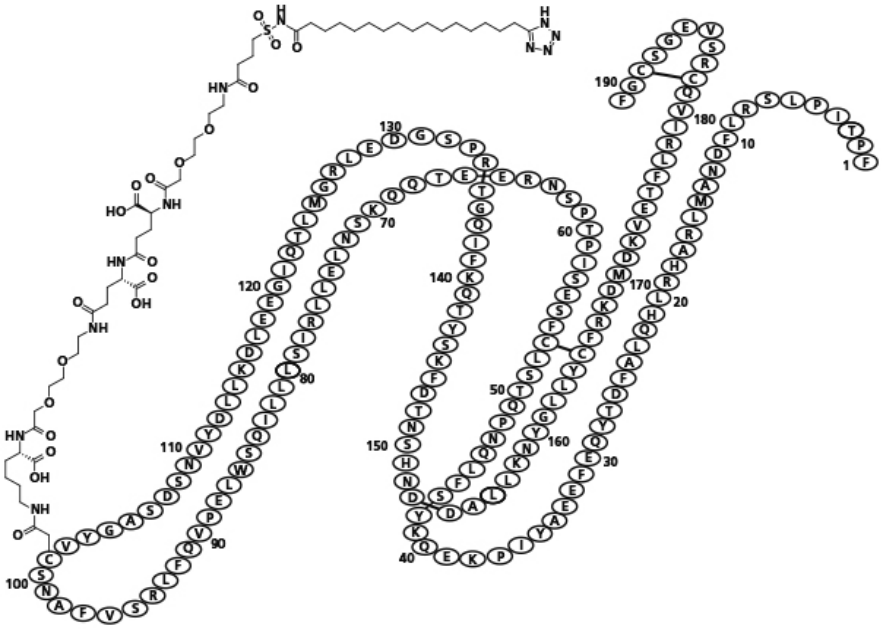
Drug Substance

Proper name: somapacitan

Chemical name: Alkylated human growth hormone L101C

Molecular formula and molecular mass: $C_{1038}H_{1609}N_{273}O_{319}S_9$; 23,290.56 Da

Structural formula:



Physicochemical properties: Sogroya® injection is supplied as a sterile, clear to slightly opalescent and colorless to slightly yellow solution.

Product Characteristics:

Somapacitan is a long-acting recombinant human growth hormone derivative produced by recombinant DNA technology in *Escherichia coli* followed by attachment of an albumin binding moiety. It consists of 191 amino acids similar to endogenous human growth hormone, with a single substitution in the amino acid backbone (L101C) to which the albumin binding moiety has been attached. The albumin binding moiety (side chain) consists of a fatty acid moiety and a hydrophilic spacer attached to position 101 of the protein.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

Clinical Trials in Pediatric Growth Hormone Deficiency (GHD)

Trial Design and Study Demographics (GHD)

Table 9 - Summary of patient demographics for clinical trials in Pediatric Growth Hormone Deficiency (GHD)

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
REAL 4 (4263)	Phase 3, Randomized, multi-center, open-label, active-controlled, parallel-group trial	Somapacitan s.c. once-weekly 0.16 mg/kg/week somatropin s.c. daily 0.034 mg/kg/day 52 weeks; + 156 weeks safety extension	200	6.4 years (2.5 - 11)	M: 149 F: 51
REAL 3 (4172)	Phase 2, Randomized, multi-center, open-label, active-controlled, parallel-group trial	Somapacitan s.c. once-weekly 0.04 mg/kg/week, 0.08 mg/kg/week and 0.16 mg/kg/week somatropin s.c. daily 0.034 mg/kg/day 26 weeks; + 26 weeks extension + 104 weeks safety extension + 208 weeks long-term safety extension	57	5.94 years (2.8 - 9.8)	M: 34 F: 23

Study Results (GHD)

The efficacy and safety of once weekly Sogroya® (5 mg/1.5 mL, 10 mg/1.5 mL and 15 mg/1.5 mL) was evaluated in a 52 weeks randomized, multi-center, open-label, active-controlled, parallel-group phase 3 trial (REAL 4) in 200 treatment-naïve, pre-pubertal pediatric patients with GHD. Patients were randomised to 0.16 mg/kg/week once weekly Sogroya® (N=132) or 0.034 mg/kg/day daily somatropin (N=68).

At baseline, the 200 patients had a mean age of 6.4 years (range: 2.5 to 11). 25.5% patients were female and 74.5% were male. 37% of patients were Asian, 0.5% were Black or African American, 57% were Caucasian, and 5.5% were categorised as 'other' or not reported. Growth hormone deficiency was idiopathic in 88% of cases and organic in 12% of cases. At baseline, patients were a mean weight of 16.5 kg, a mean height of 101.6 cm, with a baseline mean height velocity of 4.2 cm/year, mean height

standard deviation score (SDS) of -3.15 and a mean IGF-I SDS of -2.13. All patients were pre-pubertal (Tanner stage I).

The primary efficacy endpoint was the Annualized Height Velocity at 52 weeks of treatment. Results are summarized in Table 10.

Table 10 – Growth results at Week 52 in pediatric patients with GHD

Treatment Parameter	Treatment Group		Difference in Treatment
	Once weekly Sogroya® (N=132)	Daily somatropin (N=68)	Sogroya® - somatropin
ANCOVA	**LSM Estimate**	**LSM Estimate**	**LSM Difference (95% CI)**
Primary endpoint			
Annualized Height Velocity (cm/year)	11.2	11.7	-0.5 [-1.1; 0.2]*

Abbreviations: CI=confidence interval; GHD=growth hormone deficiency; LSM=least square mean; N=number of patients randomized and treated.
*The 95% CIs were obtained from the analysis of covariance (ANCOVA) model with treatment, gender, age group, region, GH peak group and gender by age group by region interaction term as factors, and baseline height as covariate. Non-inferiority will be concluded if the lower bound of the two-sided 95% CI is ≥ - 1.8

The mean Height SDS, change from baseline at 52 weeks was estimated to be 1.25 and 1.30 for Sogroya® and somatropin treatment groups, respectively.

The mean IGF-I SDS level change from baseline at 52 weeks was estimated to be 2.36 and 2.33 for Sogroya® and somatropin treatment groups, respectively.

At Week 52, there were 50.8% of Sogroya®-treated patients with an observed IGF-I SDS level between 0 and +2 and 87.1% with an observed IGF-I SDS level between -2 and +2.

There were 59 GH treatment-naïve GH-deficient pediatric patients that entered a 4-arm parallel group dose-finding trial (REAL 3) with once weekly Sogroya at dose levels of 0.04, 0.08 and 0.16 mg/kg/week or with somatropin 0.034 mg/kg/day. Of the 38 patients with 208 weeks of continuous Sogroya® treatment (with dosing at 0.16 mg/kg/week from Weeks 52 onward); the observed mean height SDS at Week 208 was -1.06 (change from baseline +2.85). Height outcome obtained at week 208 in patients switching from 0.034 mg/kg/day daily somatropin to 0.16 mg/kg/week once weekly Sogroya® at week 156 suggested that treatment effects with daily GH treatment are maintained after switching to once weekly Sogroya®.

Mean IGF-I SDS remained within the normal range for all groups.

Clinical Trials in Adult Growth Hormone Deficiency (AGHD)

Trial Design and Study Demographics (AGHD)

Table 11 – Summary of patient demographics for clinical trials in adult patients with growth hormone deficiency (AGHD)

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
REAL 1 (4054)	Phase 3, Randomised, parallel-group, placebo-(double-blinded) and active-controlled (open; Norditropin®) trial	Somapacitan s.c. once-weekly Norditropin® FlexPro® s.c. daily 35 weeks, followed by a 53-week open-label safety extension period.	300	45.1 (23–77)	M: 145 F: 155

Study Results (AGHD)

In a 35-week, double-blinded, placebo-controlled study, treatment naïve adult patients with GHD were randomised (2:1:2) and exposed to once-weekly Sogroya® 10 mg/1.5ml (N=120) or to placebo (N=61) or to daily somatropin (n=119) for a 34-week treatment period (main phase of the trial). The study was designed to assess the efficacy of Sogroya® compared to placebo.

The Sogroya® and placebo arms received weekly injections and were double-blind, while patients randomized to somatropin received open label daily injections. Patients randomized to Sogroya® or placebo received starting doses of 1.0-2.0 mg/week (according to patient characteristics; see Table 1 in 4.2 Recommended Dose and Dosage Adjustment) and those randomized to somatropin received starting doses of 0.1-0.3 mg/day. Patients underwent an 8-week titration period during which their dose was adjusted according to IGF-I levels up to 4 times. Patients remained on the dose they reached by the end of the titration period for an additional 26 weeks during the main phase of the study.

Eligible patients were aged 23-79 years with a diagnosis of GHD at least 6 months prior. Patients were required to be GH treatment-naïve or have no exposure to GH or GH secretagogues for at least 6 months prior to randomization, with a IGF-I SDS < -0.5.

Patients had a mean age of 45.1 years with the majority of patients in the age group from 23 to 64 years, 51.7% were females, and 69.7% had adult onset GHD. The mean baseline BMI was 27.4 kg/m^2. There were 66.7% White, 28.7% Asian and 2.3% Black or African American patients.

The primary endpoint was change from baseline to Week 34 in truncal fat percentage; results are shown in Table 12 below.

Table 12 - Results at 34 weeks in study 4054 (REAL 1)

Treatment Parameter[a]	Treatment Group			Difference in Treatment
	Sogroya® (N=120)	Somatropin (N=119)	Placebo (N=61)	Sogroya® - placebo
Change from baseline to week 34	**LSM Estimate**	**LSM Estimate**	**LSM Estimate**	**LSM Difference (95% CI) p-value**
Primary endpoint				
Truncal fat %	-1.06	-2.23	0.47	-1.53 [-2.68; -0.38] 0.0090[b]

Abbreviations: N = Number of subjects in FAS, CI = Confidence interval, DM Diabetes Mellitus.

[a] Body composition parameters based on dual-energy X-ray absorptiometry (DXA) scanning

[b] The primary analysis was a comparison of changes from baseline for somapacitan and placebo in truncal fat %. Changes in truncal fat % from baseline to the 34 week's measurements was analysed using an analysis of covariance model with treatment, GHD onset type, sex, region, DM and sex by region by DM interaction as factors and baseline as a covariate incorporating a multiple imputation technique where missing week 34 values were imputed based on data from the placebo group.

The mean change from baseline to week 34 in visceral adipose tissue was estimated to be a reduction of 10 cm^2 and 9 cm^2 for Sogroya® and somatropin respectively, versus an increase of 3 cm^2 for placebo.

IGF-I SDS

After 34 weeks Sogroya® increased the mean IGF-I SDS from a baseline value below -2 to a value within the reference range (-2 to +2) in treatment-naïve AGHD patients. The estimated mean IGF-I SDS level change from baseline to week 34 was 2.40, 2.37 and -0.01 for Sogroya®, somatropin and placebo arm, respectively and were similar between Sogroya® and daily somatropin.

14.4 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, include those of somapacitan or other growth hormone analogs.

No anti-somapacitan antibodies were detected in the clinical trials in adult patients with GHD.

Anti-somapacitan binding antibodies were evaluated in samples collected at baseline, week 13, and week 52 of treatment in the 52-week main period of the phase 3 trial in pediatric patients with GHD receiving somapacitan. Of the 132 pediatric patients exposed to somapacitan, 16 (12.1%) showed detectable binding antibodies to somapacitan at any time during the main period of the trial following exposure to somapacitan. 14 out of 16 patients showed detectable binding antibodies to somapacitan only at one timepoint. There was no identified clinically significant effect of anti-drug antibodies on somapacitan pharmacokinetics, pharmacodynamics, safety, or efficacy over the treatment duration.

No neutralizing antibodies to somapacitan were detected in pediatric or adult patients with GHD.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology:

In a 13-week toxicity study in rats, the animals were administered somapacitan by subcutaneous injection at doses of 0.4, 2, and 9 mg/kg body weight/day. Corresponding exposures on an AUC basis were 28-, 25-, and >1000-fold the expected maximum clinical exposure at a dose of 8 mg/week in adult patients with AGHD, and 5-, 10-, and 258-fold the expected maximum exposure at a dose of 0.16 mg/kg body weight/week in pediatric patients with GHD. The study findings were attributed to the pharmacological action of somapacitan and most findings have been reported in previous studies with human GH or other human GH products. Somapacitan administration was well tolerated until Weeks 9-10 when some males dosed with 9 mg/kg body weight/day (high-dose) showed signs of diabetes (excessive water intake and urine production, body weight loss, and increased urinary and blood plasma glucose levels). The development of diabetes symptoms led to a moribund condition that necessitated premature termination of two high dose male rats. The diabetic state also resulted in cataract formation. In surviving animals, there was an increased body weight gain, body weight, and food consumption in animals dosed at 2 and 9 mg/kg body weight/day, demonstrating a sustained pharmacological effect of somapacitan. Associated increases in organ weights were observed for many organs and, for some organs, correlated with organ enlargement. Thickened tissues were also a common macroscopic finding. A number of histopathological changes were observed in a wide range of tissues. Adverse findings of chronic progressive nephropathy (CPN) and cortical tubular casts were observed in the kidneys at 2 and 9 mg/kg body weight/day. Other histopathological findings included, but were not limited to, hypertrophy, hyperplasia, and increased collagen content in many tissues at all doses, bilateral lenticular degeneration in the eyes at the high-dose (correlating with cataract formation), dilated brain ventricles and islet cell atrophy/degeneration in the pancreas at the high-dose, reduced cellularity of the pars distalis and myocardial degeneration at 2 and 9 mg/kg body weight/day, effects on bone at 2 and/or 9 mg/kg body weight/day (increased trabecular bone, chondroid hyperplasia of growth plates, increased height of articular cartilage), feminization of male mammary tissue at all doses, increased secretory activity in male and female mammary tissue at all doses, and effects in the gonads of both sexes (e.g., reduction in the number of spermatozoa, degenerate spermatogenic cells in ducts, bilateral seminiferous tubular atrophy in males correlating with small epididymides and testes at 2 and 9 mg/kg body weight/day; increase in size of corpora lutea in females at 2 and 9 mg/kg body weight/day correlating with enlarged ovaries at all doses). While findings were generally consistent with the pharmacological effects of somapacitan, the findings were considered adverse at all dose levels. A NOAEL could not be determined due to the presence of adverse effects at all dose levels.

In a 26-week study in rats, the dose levels were 1, 2, and 4 mg/kg body weight, and the dosing regimen was changed to twice weekly dosing to investigate whether a reduced frequency of dosing ameliorated the pro-diabetic effects. Corresponding exposures on an AUC basis were 4-, 10-, and 36-fold the expected maximum clinical exposure at a dose of 8 mg/week in adult patients, and 0.7-, 2-, and 6-fold the expected maximum exposure at a dose of 0.16 mg/kg body weight/week in pediatric patients. Somapacitan-related findings were observed at all doses and were similar to those observed in the 13-week study. However, diabetes and CPN were not observed and the extent of the adverse effects,

including the range of tissues affected, was reduced in severity owing to the lower doses tested and the less frequent dosing regimen. However, a NOAEL could not be determined due to the presence of adverse effects at all dose levels.

In a 26-week study in cynomolgus monkeys, animals were administered somapacitan by subcutaneous injection at doses of 0.2, 2, and 9 mg/kg body weight twice weekly. Corresponding exposures on an AUC basis were 207-, >1000-, and >5000-fold the expected maximum clinical exposure at a dose of 8 mg/week in adult patients, and 33-, 269-, and >1000-fold the expected maximum exposure at a dose of 0.16 mg/kg body weight/week in pediatric patients. Somapacitan administration resulted in increased body weight gain and body weight at all doses in males only. Somapacitan administration also resulted in mammary gland findings; mammary gland swelling and lactation was observed in both females and males at all doses and correlated macroscopically with mammary gland thickening and cysts in females at all doses, as well as with histopathological findings of acinar and ductular dilation and papillary hyperplasia of the acinar epithelium in females at all doses and ductular dilation in males at all doses. No other notable effects were observed, including no adverse effects on cardiovascular function. The mammary gland findings were considered adverse at all doses, and therefore, a NOAEL could not be determined.

Carcinogenicity: No carcinogenicity studies have been performed with somapacitan.

Genotoxicity: No genotoxic potential was identified in the *in vitro* or *in vivo* studies conducted with somapacitan. Somapacitan was non-mutagenic in the bacterial reverse mutation test and non-genotoxic in the *in vitro* chromosomal aberration test conducted in primary human peripheral blood lymphocytes and the *in vivo* erythrocyte micronucleus test conducted in rats.

Reproductive and Developmental Toxicology: Reproductive and developmental toxicity studies were conducted in rats and rabbits using the subcutaneous route of administration. In all studies, somapacitan induced increases in body weights, weight gain, and/or food consumption in paternal and maternal animals. However, no overt maternal toxicity was observed in any study.

Effects of somapacitan on male fertility and on female fertility/early embryonic development were assessed in rats in separate studies. In each study, male or female rats were administered somapacitan at doses of 0 (vehicle control), 1, 2, or 4 mg/kg body weight twice weekly from prior to mating, during, mating, and post-mating (males) or during gestation until gestation day (GD) 7 (females). Corresponding exposures on an AUC basis were for males 4-, 10-, and 32-fold and for females 4-, 17-, and 39-fold the expected maximum clinical exposure at a dose of 8 mg/week in adults, respectively. No adverse effects were observed on male and female fertility or on early embryonic development in rats. The NOAEL for effects on fertility and early embryonic development in rats was therefore 4 mg/kg body weight twice weekly (the highest dose tested). However, somapacitan induced irregular estrus cycles and longer estrus cycles in females at all doses.

Effects of somapacitan on embryo-fetal development were assessed in rats and rabbits following maternal exposure during the period of organogenesis. In rats, females were administered somapacitan at doses of 0 (vehicle control), 2, 6, or 18 mg/kg body weight/day using a divided dosing regimen where animals were dosed from GD 6 to 9, GD 10 to 13, or GD 14 to 17. Corresponding exposures on an AUC basis were 5-, 24-, and 305-fold the expected maximum clinical exposure at a dose of 8 mg/week in adults, respectively. Fetal weights were increased slightly at all doses. At the high-dose of 18 mg/kg body weight/day, fetal skeletal malformations consisting of short/bent/thickened long bones were observed. Similar findings were not observed at the lower

doses. The NOAEL for embryo-fetal developmental toxicity in rats was therefore 6 mg/kg body weight/day based on the fetal skeletal malformations observed at the high-dose.

In the embryo-fetal development study conducted in rabbits, females were administered somapacitan at doses of 0 (vehicle control), 1, 3, or 9 mg/kg body weight every two days from GD 6 to 18. Corresponding exposures on a C_{12hour} basis were 17-, 73, and 1132-fold the expected maximum clinical exposure at a dose of 8 mg/week in adults. No test article-related fetal malformations were observed. However, a dose-dependent and adverse reduction in fetal weights was observed at all doses. A NOAEL for embryo-fetal developmental toxicity in rabbits was therefore not determined.

Effects of somapacitan on pre- and post-natal development were assessed in rats. Female rats were administered somapacitan at doses of 0 (vehicle control), 4, 9, or 18 mg/kg body weight twice weekly from GD 6 to post-natal day (PND) 18. Corresponding exposures on an AUC basis were 57-, 342-, and 787-fold the expected maximum clinical exposure at a dose of 8 mg/week in adults. F1 offspring were not administered somapacitan directly. No adverse effects on post-natal development were observed in offspring, including no effects on neurobehavioural endpoints, sexual maturation, and reproduction. Increased body weights were observed in F1 offspring during the pre-weaning period at all maternal dose levels but resolved post-weaning. An increased incidence of renal pelvic dilatation was also observed in F1 offspring at the time of weaning on PND 21 at all doses, but evidence of recovery was observed as a similar finding was not observed in F1 adult animals. The NOAEL for effects on pre- and post-natal development in rats was therefore 18 mg/kg body weight twice weekly (the highest dose tested). However, maternal administration of somapacitan resulted in acyclic estrus cycles in F1 female offspring at the high-dose of 18 mg/kg body weight. In addition, somapacitan was observed in F1 plasma on PND 4 following maternal exposure at the high-dose but not thereafter.

Somapacitan and/or its metabolites have been detected in rat fetal tissues (highest concentration in fetal kidneys) following administration to pregnant rats, indicating transfer across the placental barrier.

Somapacitan and/or its metabolites have also been detected in rat milk following administration to rats during lactation, indicating excretion in milk.

Juvenile Toxicity: No juvenile toxicity studies have been performed with somapacitan.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]SOGROYA®

Somapacitan injection

Read this carefully before you start taking **Sogroya®** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Sogroya®**.

What is Sogroya® used for?

- Sogroya® is used for the long-term treatment of children and adolescents who are not growing because of low growth hormone levels.
- Sogroya® also replaces the growth hormone in adults with growth hormone deficiency.

How does Sogroya® work?

Sogroya® contains the active substance 'somapacitan'.

- Somapacitan is a long-acting version of the natural growth hormone produced by the body with a single amino acid substitution.
- Somapacitan is made by 'recombinant DNA technology' meaning from cells that have received a gene (DNA) that makes them produce growth hormone. In Sogroya®, a small side-chain has been attached to the growth hormone which links Sogroya® to the protein (albumin) naturally found in the blood to slow down its removal from the body allowing the medicines to be given less often.

What are the ingredients in Sogroya®?

Medicinal ingredients: somapacitan

Non-medicinal ingredients: histidine, hydrochloric acid (as needed), mannitol, phenol, poloxamer 188, sodium hydroxide (as needed) and water for injection

Sogroya® comes in the following dosage forms:

Sogroya® is available as a pre-filled disposable pen in 3 colour coded strengths:

- 5 mg / 1.5 mL pen with a teal pen cap and dose button
- 10 mg / 1.5 mL pen with a yellow pen cap and dose button
- 15 mg / 1.5 mL pen with a rubine red pen cap and dose button

Do not use Sogroya® if:

- If you are **allergic** to 'somapacitan' or 'phenol' or any of the other ingredients of Sogroya® (see **What are the ingredients in Sogroya®?**).
- If you have a **tumour** which is growing. You must have finished your anti-tumour treatment before you start your Sogroya® treatment. Sogroya® must be discontinued if the tumour grows.

- (Adults only) If you have had **open heart surgery** or **abdominal surgery**.
- (Adults only) If you have **serious accidental injury, severe breathing problems**.
- (Children only) If your bones have already finished growing (this is called closure of the growth plates).
- (Children only) If you have Prader-Willi syndrome and are severely obese or have breathing problems, including sleep apnea.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Sogroya®. Talk about any health conditions or problems you may have, including if you:

- have ever had any kind of cancer or another kind of **tumour**.
- have **high blood sugar** (hyperglycemia) as your blood sugar may need to be checked regularly and the dose of your diabetes medicines may need to be adjusted.
- have a **replacement therapy with glucocorticoids**, because you have been told your body does not produce enough (adrenocortical insufficiency). You should consult your doctor regularly, as you may need adjustment of your glucocorticoid dose.
- have severe **headaches**, **eyesight problems**, **nausea**, or **vomiting** as these could be symptoms of increased pressure in the brain (benign intracranial hypertension) as your treatment may need to be stopped.
- have **thyroid problems**, your thyroid hormones need to be checked regularly and your dose of thyroid hormone may need to be adjusted.
- (Adults only) are a woman taking hormonal replacement therapy with estrogen, your dose of Sogroya® may need to be higher. If you stop using oral estrogen, your dose of Sogroya® may need to be reduced. Your doctor may recommend you to change to a vaginal hormone product or a hormone patch.
- are pregnant or plan to become pregnant. It is not known if Sogroya® will harm your unborn baby. Talk to your healthcare provider if you are pregnant or plan to become pregnant.
- are breastfeeding or plan to breastfeed. It is not known if Sogroya® passes into your breast milk. You and your healthcare provider should decide if you will take Sogroya® while you breastfeed.
- have **scoliosis**. Growth hormone treatment increases growth rate, and progression of pre-existing scoliosis can occur.
- (children only) **have hip or knee pain**, or begin to **limp** while on treatment.
- have changes in **skin** colour or in the appearance of birthmarks or **moles** on the skin.

Other warnings you should know about:

Thickening of skin
If you inject Sogroya® at the same site for a long period, thickened skin may appear where you inject your medicine. Change the place of injection on your body from one week to the next.

Antibodies
Antibodies against somapacitan may occur as it happens with other growth hormone treatments. If your healthcare professional suspects you have developed these antibodies, they may test you for antibodies against somapacitan.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Sogroya®:

- **Glucocorticoids** such as hydrocortisone, dexamethasone and prednisolone
- **Estrogen** as part of the oral hormonal replacement therapy
- **Male sex hormones** (androgen medicines) such as testosterone
- **Gonadotropin** medicines (gonad stimulating hormone) which stimulate the production of sex hormones
- **Insulin** or other diabetes medicines
- **Thyroid** hormone medicines such as thyroxine and levothyroxine
- **Anticonvulsants** medicines – such as carbamazepine and diazepam
- **Cyclosporine** (immunosuppressive) – a medicine to suppress your immune system

How to take Sogroya®:

Always use this medicine exactly as your healthcare professional has told you. Check with your healthcare professional if you are not sure.

Sogroya® is given as an injection under the skin (subcutaneous injection). Do not inject it into a vein or muscle. Before you use the pen for the first time, your doctor or nurse will show you how to use it. The best places to give the injection are:

- the front of your thighs
- the front of your waist (abdomen)
- the buttocks
- the upper arms (children only)

Change the place on your body where you inject into every week.

For detailed instructions on how to inject Sogroya®, please see **Instructions for Use**.

<u>When to use Sogroya®</u>

- You should use Sogroya® once a week on the same day each week if possible.
- You can give yourself the injection at any time of the day.

If you are changing from another weekly growth hormone therapy to Sogroya®, you are advised to continue your usual once weekly dosing schedule.

If you are changing from daily growth hormone therapy to Sogroya® choose the preferred day for the weekly dose and stop final dose of daily treatment the day before (or at least 8 hours before) taking the first dose of Sogroya®.

Changing from another type or brand of growth hormone should be done by your healthcare professional.

On occasions when administration at the scheduled dosing day is not possible, you can take Sogroya® up to 2 days before or 3 days after your scheduled dosing day. The next dose you can take as usual the following week.

If necessary, you can change the day of your weekly injection of Sogroya® as long as it has been at least 4 days since your last injection of it. After selecting a new dosing day, continue with once a week dosing.

How long you will need treatment for

You may need Sogroya® for as long as your body does not produce enough growth hormone

- If you are taking Sogroya® for growth failure you will continue using Sogroya® until you stop growing.
- If you still lack growth hormone after you stop growing, you may need to continue using Sogroya® into adulthood.
- Do not stop using Sogroya® without discussing this with your healthcare professional first.

Usual dose:

Children and adolescents

The dose for children and adolescents depends on their body weight. The recommended dose of Sogroya® is 0.16 mg per kg body weight given once a week. Your child's dose may be lowered from the recommended dose according to blood test results, as necessary.

Adults

The usual starting dose is 1.5 mg once a week if you get growth hormone treatment for the first time and if you are already in treatment with daily growth hormone (somatropin medicine). If you are a woman taking oral estrogen (hormonal replacement therapy) you may need a higher dose of Sogroya®. If you are above 60 years, you may need a lower dose. See Table 1 below.

Table 1: Starting dose recommendation

Adult growth hormone deficiency	Recommended starting dose
You are between 18-60 years	1.5 mg/week
You are a woman on oral estrogen therapy regardless of age	2 mg/week
You are 60 years or above	1 mg/week

Your doctor may increase or decrease your dose step by step and regularly until you are on the right dose based on your individual needs and your experience of side effects.

- Do not take more than a maximum of 8 mg once a week.
- Do not change your dose unless your doctor has told you to.

After you have reached your right dose, your doctor will evaluate your treatment every 6 to 12 months. You may need to have your body mass index checked and blood samples taken.

If you have any further questions on the use of this medicine, ask your healthcare professional.

Overdose:

If you think you, or a person you are caring for, have taken too much Sogroya®, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you forget to inject a dose:

- and it is 3 days or less after you should have used Sogroya®, use it as soon as you remember. Then inject your next dose as usual the following week.
- and it is more than 3 days since you should have used Sogroya®, skip the missed dose. Then inject your next dose as usual on your next scheduled day.

Do not take an extra dose or increase the dose to make up for a missed dose.

What are possible side effects from using Sogroya®?

These are not all the possible side effects you may have when taking Sogroya®. If you experience any side effects not listed here, tell your healthcare professional.

Side effects seen in children and adolescents
Very common: may affect more than 1 in 10 people

- **Headache**

Common: may affect up to 1 in 10 people

- **Swollen hands and feet** due to **fluid retention**
- Decreased thyroid hormone (hypothyroidism)
- Redness and pain in the area of injection
- **Joint pain**
- **High blood sugar** (hyperglycemia)
- Feeling very tired (fatigue)
- The **adrenal glands do not make enough steroid hormones** (adrenocortical insufficiency)

Side effects seen in adults
Very common: may affect more than 1 in 10 people

- **Headache**

Common: may affect up to 1 in 10 people

- **Swollen hands and feet** due to **fluid retention**
- Decreased thyroid hormone (hypothyroidism)
- The **adrenal glands do not make enough steroid hormones** (adrenocortical insufficiency)
- Feeling very tired or weak (fatigue or asthenia)
- Redness and pain in the area of injection
- **High blood sugar** (hyperglycemia)
- **Joint pain**
- Feeling of **'pins and needles'** mainly in fingers

Uncommon: may affect up to 1 in 100 people

- **Thickening of skin** where you **inject** your medicine (lipohypertrophy)
- **Numb feeling and tingling in your hand(s)** (carpal tunnel syndrome)

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON			
Headache	✓		
COMMON			
Swollen hands and feet due to fluid retention	✓		
Decreased thyroid hormone (hypothyroidism)	✓		
Redness and pain in the area of injection	✓		
Joint pain	✓		
High blood sugar (hyperglycemia)	✓		
Feeling very tired or weak (fatigue or asthenia)	✓		
The adrenal glands do not make enough steroid hormones (adrenocortical insufficiency).	✓		
Feeling of 'pins and needles' mainly in fingers	✓		
RARE			
Thickening of skin where you inject your medicine (lipohypertrophy)	✓		
Numb feeling and tingling in your hand(s) (carpal tunnel syndrome)	✓		

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

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.

Storage:

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

Before opening*

- Store in refrigerator (2°C - 8°C).
- Do not freeze or expose to heat.
- Keep away from the cooling element inside the fridge.
- Do not use Sogroya® if it has been frozen.
- Keep unused (unopened) Sogroya® in the carton so that it stays clean and protected from light.
- If you are not able to store in a refrigerator before opening Sogroya®:
    - you can keep it at room temperature, 30°C and below for a maximum of 72 hours (3 days). This is as long as you keep Sogroya® as cool as possible and away from direct heat and light.
    - place Sogroya® in the refrigerator after this period of keeping it at room temperature.

During use*

- You can keep the pen for 6 weeks when stored in a refrigerator (2°C - 8°C).
- Keep away from the cooling element.
- Do not freeze.
- If you are not able to store the opened Sogroya® in a refrigerator:
    - it can be kept at room temperature, 30°C and below for a maximum of 72 hours (3 days). This is as long you keep it as cool as possible and away from direct heat and light.
    - return Sogroya® in the refrigerator after period of use at room temperature.

When you are not using the pen, keep the Sogroya® in the outer carton with pen cap on to protect from light.

Always remove the injection needle after each injection and store the pen without a needle attached.

***The total time allowed at room temperature, 30°C and below is 72 hours (3 days). This is regardless of whether the product is in-use (opened) or not in-use (unopened).**
Do not use this medicine if the solution does not appear clear to slightly opalescent, colourless to slightly yellow and free from visible particles. 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 protect the environment.

Keep out of reach and sight of children.

If you want more information about Sogroya®:

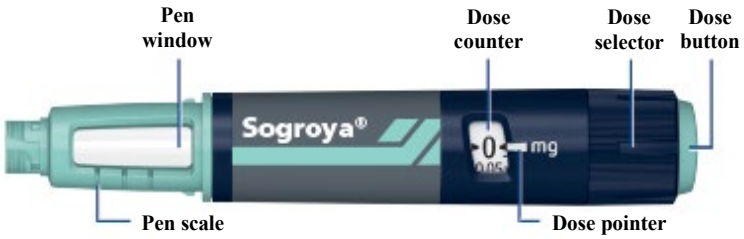
- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website (http://www.novonordisk.ca), or by calling 1-800-465-4334.

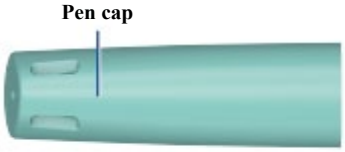
This leaflet was prepared by Novo Nordisk Canada Inc.

Last Revised: 2023

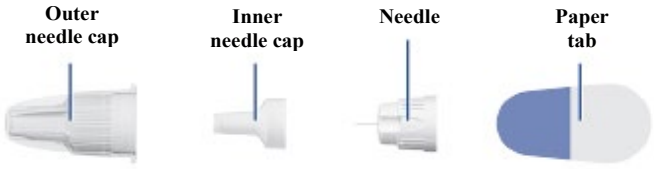
Instructions for Use

Overview of Sogroya® pen





Needle (example)



How to use your once weekly Sogroya® pen

5 steps you should follow for a Sogroya® injection:
Step 1. Prepare your Sogroya® pen

Step 2. Check the flow with each new pen

Step 3. Select your dose

Step 4. Inject your dose

Step 5. After your injection

For further information about your pen: see sections *Frequently Asked Questions, Important information, Patient Information*
Please read these instructions carefully before using your Sogroya® prefilled pen.

⚠ Pay special attention to these notes as they are important for safe use of the pen.

ⓘ Additional information

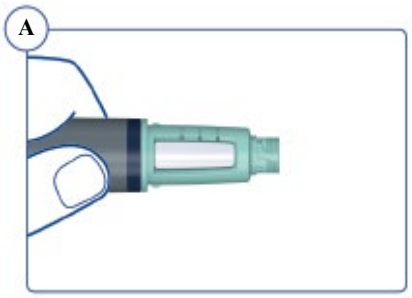
Sogroya® is a prefilled growth hormone pen. It contains 5 mg of Sogroya® and delivers doses from 0.025 mg to 2 mg, in increments of 0.025 mg. Sogroya® is for use under the skin only (subcutaneous). Sogroya® prefilled pen is designed to be used with NovoFine® disposable needles up to a length of 8 mm.

Do not share your Sogroya® pen and needles with another person. You may give another person an infection or get an infection from them.

Do not use your pen without proper training from your doctor or nurse. Make sure that you are confident in making an injection with the pen before you start your treatment. If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help. Get help from a person with good eyesight who is trained to use the pen.

Step 1. Prepare your once weekly Sogroya® pen

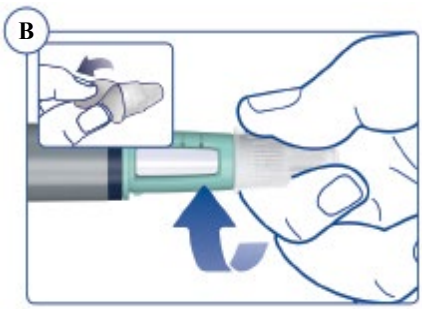
- Wash your hands with soap and water.
- **Check the name, strength, and coloured label** on your pen to make sure that it contains Sogroya® in the right strength.
- Pull off the pen cap.
- Turn the pen upside down once or twice to check that the Sogroya® in your pen is clear and colourless. See figure A. **If the Sogroya® looks cloudy, do not use the pen.**



⚠ Make sure the right pen is used. Especially if you use more than one type of injectable medicine. Using the wrong medicine could be harmful to your health.

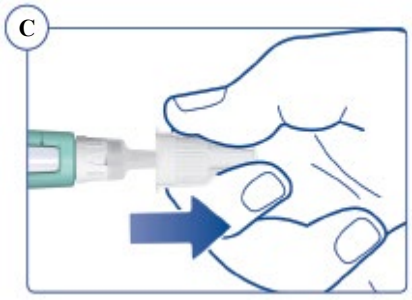
When you are ready to take your injection

- Firstly, take a new disposable needle and tear off the paper tab.
- Then push the needle straight onto the pen. Turn the needle clockwise **until it is on tight.** See figure B.



- Pull off the outer needle cap and keep it for later. You will need it after the injection, to safely remove the needle from the pen. See figure C.

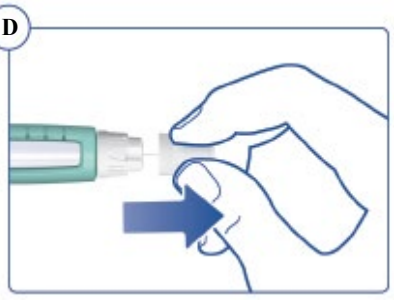
ⓘ The needle is covered by two caps. You must remove both caps. If you forget to remove both caps you will not inject any medicine.



- Pull off the inner needle cap and dispose of it. If you try to put it back on, you may accidentally stick yourself with the needle. See figure D.

ⓘ A drop of Sogroya® may appear at the needle tip. This is normal, but you must still check the flow with each new pen. See step 2.

D



⚠ **Always use a new needle for each injection.** This reduces the risk of contamination, infection, leakage of Sogroya®, and blocked needles leading to incorrect dosing.

⚠ Never use a bent or damaged needle.

Step 2. Check the flow with each new pen

ⓘ **If your pen is already in use,** proceed to step 3.

- **Before using a new pen,** check the flow to make sure Sogroya® can flow through the pen and needle.
- Turn the dose selector clockwise one tick mark to select 0.025 mg. You may hear a faint click. See figure E.

E

- **One tick mark equals 0.025 mg** in the dose counter. See figure F.

F

- Hold the pen with the needle pointing up. Press and hold in the dose button until the dose counter returns to "0". **The "0" must line up with the dose pointer.** See figure G.

G

- Check that a drop of Sogroya® appears at the needle tip. See figure H.

ⓘ **If no Sogroya® appears,** repeat step 2 up to 6 times.

If you still do not see a drop of Sogroya®, **change the needle.** Remove the needle as described in step 5 and repeat step 1 and 2 again.

Do not use the pen if a drop of Sogroya® still does not appear after repeating step 2.

H

Step 3. Select your dose

- To start, check that the dose counter is set at "**0".**
- Turn the dose selector clockwise to select the dose you need. See figure I.

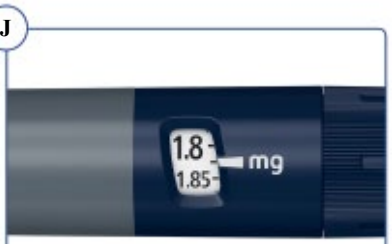
When you have selected your dose, you can proceed to step 4.

ⓘ **If there is not enough Sogroya® left** to select a full dose, *see Frequently Asked Questions.*

I

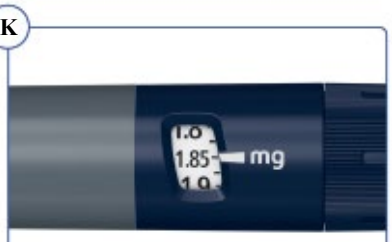
ⓘ The dose counter shows the dose in mg. See figures J and K. Always use the dose pointer to select the exact dose. **Do not count the pen clicks. Do not use the pen scale.**

J

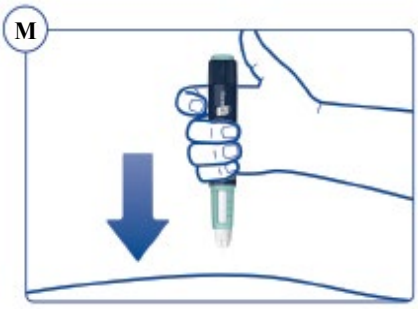
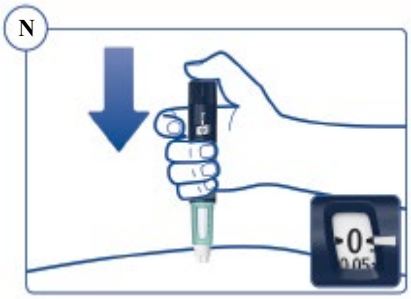
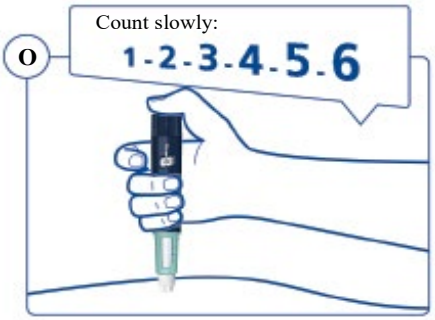


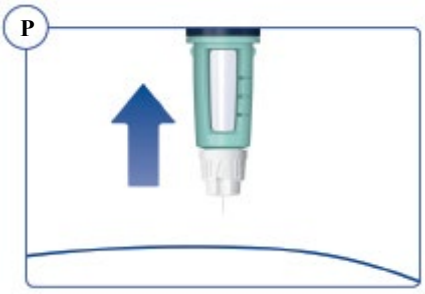
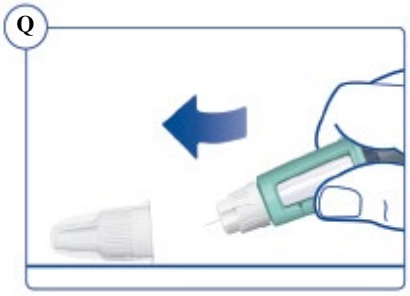
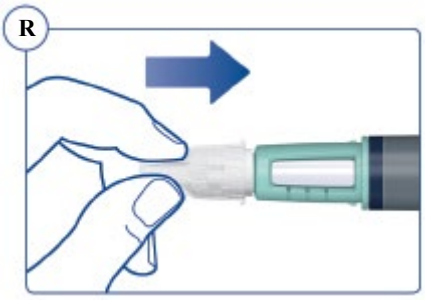
Example: 1.825 mg selected

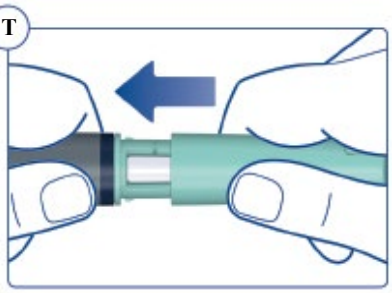
K



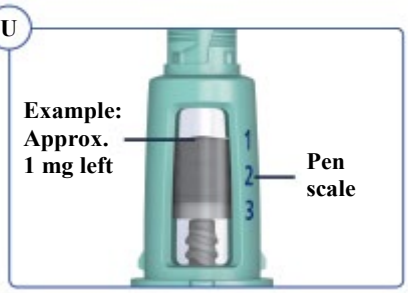
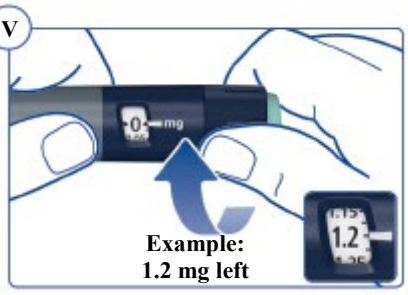
Example: 1.85 mg selected

ⓘ If you select the wrong dose, you can turn the dose selector clockwise or counterclockwise to the correct dose. See figure L. The pen clicks sound and feel differently when the dose selector is turned clockwise, counterclockwise, or if you accidentally force it past the number of mg left.	L 
Step 4. Inject your dose	
• Insert the needle into your skin as your doctor or nurse has shown you. See figure M. Make sure you can see the dose counter. **Do not cover it with your fingers.** This could block the injection. ⓘ **Remember to change the injection site every week.**	M 
• **Press and hold down the dose button until the dose counter shows "0". Keep pressing the dose button with the needle in your skin and slowly count to 6**. See figure N and O. The "0" must line up with the dose pointer. You may then hear or feel a click. ⓘ If "0" does not appear in the dose counter after continuously pressing the dose button, your needle or pen may be blocked or damaged, see *Frequently Asked Questions.*	N  O 
• Carefully remove the needle from your skin. See figure P. If blood appears at the injection site, press lightly. Do not rub the area. ⓘ You may see a drop of Sogroya® at the needle tip after injecting. This is normal and does not affect your dose.	

	P 
Step 5. After your injection	
• Insert the needle tip into the outer needle cap on a flat surface without touching the needle or the outer needle cap. See figure Q.	Q 
• Once the needle is covered, carefully push the outer needle cap completely on. See figure R.	R 
• Unscrew the needle and dispose of it carefully as instructed by your doctor, nurse, pharmacist or local authorities. **Always dispose of the needle after each injection.** When the pen is empty, throw it away **without** a needle on as instructed by your doctor, nurse, pharmacist or local authorities. The pen cap and the empty carton can be disposed of in your household trash.	S 
• Put the pen cap on your pen after each use to protect Sogroya® from direct light. See figure T. To store your pen, see *'Storage'* in the *Patient Medication Information*.	

<table>
<tr><td></td><td>T
  </td></tr>
<tr><td colspan="2">⚠ Do not try to put the inner needle cap back on.
You may stick yourself with the needle.

⚠ Always remove the needle from your pen immediately after each injection. This reduces the risk of contamination, infection, leakage of Sogroya®, and blocked needles leading to incorrect dosing.</td></tr>
<tr><td colspan="2">Frequently Asked Questions</td></tr>
<tr><td>How do I see how much Sogroya® is left in my pen?

The pen scale shows you approximately how much Sogroya® is left in your pen. See figure U.</td><td>U
 
</td></tr>
<tr><td>To see how much Sogroya® is left, use the dose counter: Turn the dose selector clockwise until the dose counter stops. You can select a maximum dose of 2 mg. If it shows “2”, at least 2 mg are left in your pen.
If the dose counter stops at “1.2”, only 1.2 mg are left in your pen. See figure V.</td><td>V
 
</td></tr>
<tr><td>What if I need a larger dose than what is left in my pen?</td><td>It is not possible to select a larger dose than the amount of mg left in your pen.
If you need more Sogroya® than you have left in your pen, you can use a new pen or split your dose between your current pen and a new pen. Only if trained or advised by your doctor or nurse, may you split your dose. Use a calculator to plan the doses as instructed by your doctor or nurse.

Be very careful to calculate correctly, otherwise it may lead to medication error. If you are not sure how to split your dose using two pens, then select and inject the dose you need with a new pen.</td></tr>
</table>

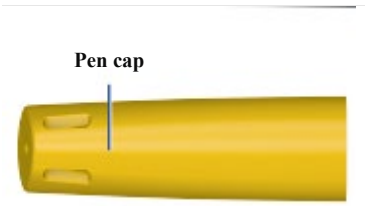
What if no Sogroya® appears when I check the flow?	**A. Your needle may be blocked or damaged,** if no Sogroya® appears at the needle tip. Remove the needle as described in step 5 and repeat steps 1 and 2. **B. Your pen may be defective,** if Sogroya® still does not appear after changing the needle. Do not use the pen.
What if "0" does not appear after completing my injection?	In this case the needle or pen may be blocked or damaged, and **you have not received any Sogroya®** – even though the dose counter has moved from the original dose that you have set. Remove the needle as described in step 5 and repeat steps 1 to 4.
How should I take care of my pen?	Be careful not to drop your pen or knock it against hard surfaces. Do not expose your pen to dust, dirt, liquid, or direct light. If there is Sogroya® left in the pen, store the pen as directed in *'Storage'* in the *Patient Medication Information.* Do not try to refill your pen, it is prefilled and must be disposed of when empty.
What if I drop my pen?	If you drop your pen or think that something is wrong with it, attach a new disposable needle and check the flow before you inject, see steps 1 and 2. If your pen has been dropped, check the cartridge, if the cartridge is cracked, do not use the pen. Do not try to repair your pen or pull it apart.
How do I clean my pen?	Do not wash, soak, or lubricate your pen. It may be cleaned with a mild detergent on a moistened cloth.

Important information

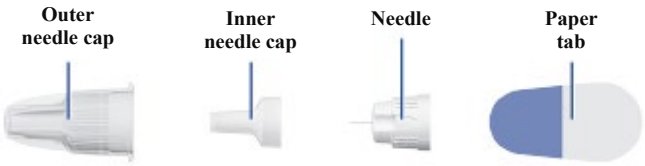
- Caregivers must be very careful when handling needles – to reduce the risk of needle sticks and cross-infection.
- Always keep your pen and needles out of reach of others, especially children.
- **Do not use the pen** if it is damaged. Do not try to repair your pen or pull it apart.
- To store your pen, *see 'Storage'* in the *Patient Medication Information.*

Instructions for Use

Overview Sogroya® pen



Needle (example)



How to use your once weekly Sogroya® pen

5 steps you should follow for a Sogroya® injection:

Step 1. Prepare your Sogroya® pen

Step 2. Check the flow with each new pen

Step 3. Select your dose

Step 4. Inject your dose

Step 5. After your injection

For further information about your pen: see sections *Frequently Asked Questions, Important information, Patient Information*

Please read these instructions carefully before using your Sogroya® prefilled pen.

⚠ Pay special attention to these notes as they are important for safe use of the pen.

ⓘ Additional information

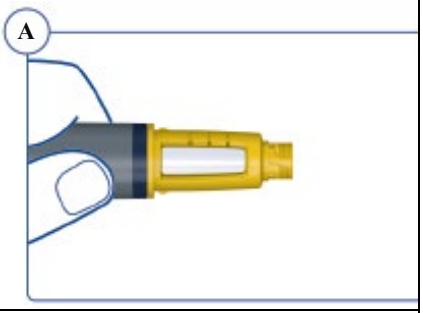
Sogroya® is a prefilled growth hormone pen. It contains 10 mg of Sogroya® and delivers doses from 0.05 mg to 4 mg, in increments of 0.05 mg. Sogroya® is for use under the skin only (subcutaneous). Sogroya® prefilled pen is designed to be used with NovoFine® disposable needles up to a length of 8 mm.

Do not share your Sogroya® pen and needles with another person. You may give another person an infection or get an infection from them.

Do not use your pen without proper training from your doctor or nurse. Make sure that you are confident in making an injection with the pen before you start your treatment. If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help. Get help from a person with good eyesight who is trained to use the pen.

Step 1. Prepare your once weekly Sogroya® pen

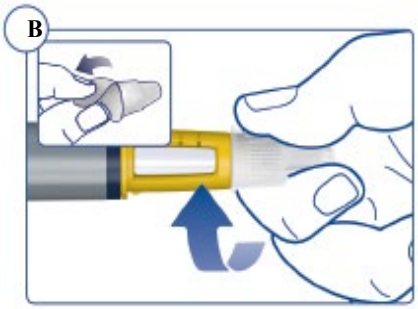
- Wash your hands with soap and water.
- **Check the name, strength, and coloured label** on your pen to make sure that it contains Sogroya® in the right strength.
- Pull off the pen cap.
- Turn the pen upside down once or twice to check that the Sogroya® in your pen is clear and colourless. See figure A. **If the Sogroya® looks cloudy, do not use the pen.**



⚠ Make sure the right pen is used. Especially if you use more than one type of injectable medicine. Using the wrong medicine could be harmful to your health.

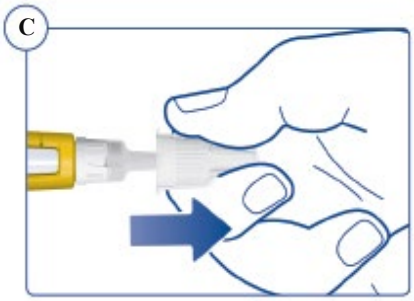
When you are ready to take your injection

- Firstly, take a new disposable needle and tear off the paper tab.
- Then push the needle straight onto the pen. Turn the needle clockwise **until it is on tight.** See figure B.



- Pull off the outer needle cap and keep it for later. You will need it after the injection, to safely remove the needle from the pen. See figure C.

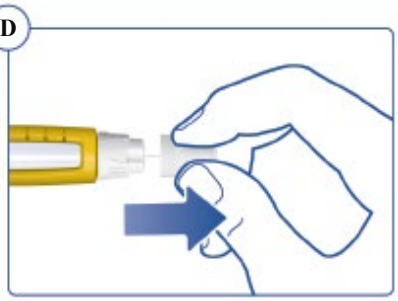
ⓘ The needle is covered by two caps. You must remove both caps. If you forget to remove both caps you will not inject any medicine.



- Pull off the inner needle cap and dispose of it. If you try to put it back on, you may accidentally stick yourself with the needle. See figure D.

A drop of Sogroya® may appear at the needle tip. This is normal, but you must still check the flow with each new pen. See step 2.

D



Always use a new needle for each injection. This reduces the risk of contamination, infection, leakage of Sogroya®, and blocked needles leading to incorrect dosing.

Never use a bent or damaged needle.

Step 2. Check the flow with each new pen

If your pen is already in use, proceed to step 3.

- **Before using a new pen,** check the flow to make sure Sogroya® can flow through the pen and needle.
- Turn the dose selector clockwise one tick mark to select 0.05 mg. You may hear a faint click. See figure E.

E

- **One tick mark equals 0.05 mg** in the dose counter. See figure F.

F

- Hold the pen with the needle pointing up. Press and hold in the dose button until the dose counter returns to "0". **The "0" must line up with the dose pointer.** See figure G.

G

- Check that a drop of Sogroya® appears at the needle tip. See figure H.

If no Sogroya® appears, repeat step 2 up to 6 times.

If you still do not see a drop of Sogroya®, **change the needle.** Remove the needle as described in step 5 and repeat step 1 and 2 again.

Do not use the pen if a drop of Sogroya® still does not appear after repeating step 2.

H

Step 3. Select your dose

- To start, check that the dose counter is set at "**0".**
- Turn the dose selector clockwise to select the dose you need. See figure I.

When you have selected your dose, you can proceed to step 4.

If there is not enough Sogroya® left to select a full dose, *see Frequently Asked Questions.*

I

The dose counter shows the dose in mg. See figures J and K. Always use the dose pointer to select the exact dose. **Do not count the pen clicks. Do not use the pen scale.**

J

Example: 2.95 mg selected

K

Example: 0.7 mg selected

If you select the wrong dose, you can turn the dose selector clockwise or counterclockwise to the correct dose. See figure L.

The pen clicks sound and feel differently when the dose selector is turned clockwise, counterclockwise, or if you accidentally force it past the number of mg left.

L

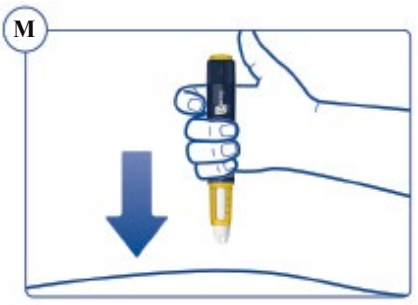
Step 4. Inject your dose

- Insert the needle into your skin as your doctor or nurse has shown you. See figure M.

  Make sure you can see the dose counter. **Do not cover it with your fingers.** This could block the injection.

Remember to change the injection site every week.

M

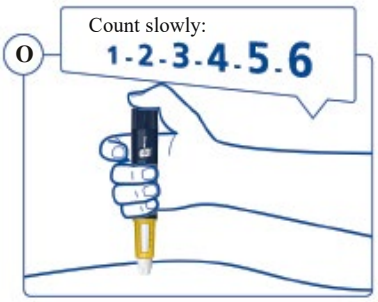


- **Press and hold down the dose button until the dose counter shows "0". Keep pressing the dose button with the needle in your skin and slowly count to 6.** See figure N and O.
  The "0" must line up with the dose pointer. You may then hear or feel a click.

If "0" does not appear in the dose counter after continuously pressing the dose button, your needle or pen may be blocked or damaged, see *Frequently Asked Questions.*

N

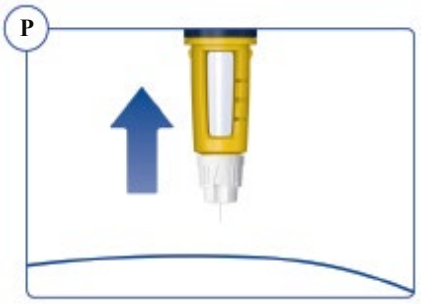
O



- Carefully remove the needle from your skin. See figure P. If blood appears at the injection site, press lightly. Do not rub the area.

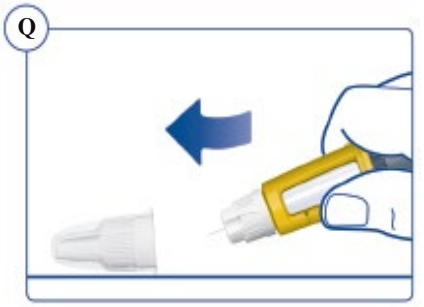
You may see a drop of Sogroya® at the needle tip after injecting. This is normal and does not affect your dose.

P

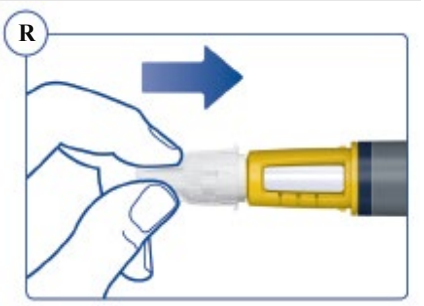


Step 5. After your injection

- Insert the needle tip into the outer needle cap on a flat surface without touching the needle or the outer needle cap. See figure Q.



- Once the needle is covered, carefully push the outer needle cap completely on. See figure R.



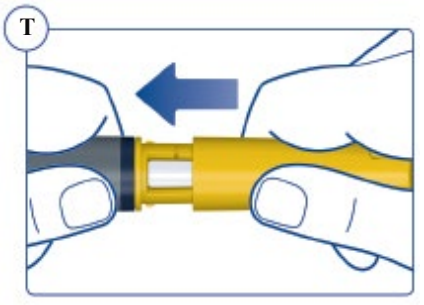
- Unscrew the needle and dispose of it carefully as instructed by your doctor, nurse, pharmacist or local authorities.

  Always dispose of the needle after each injection.
  When the pen is empty, throw it away **without** a needle on as instructed by your doctor, nurse, pharmacist or local authorities.

  The pen cap and the empty carton can be disposed of in your household trash.

- Put the pen cap on your pen after each use to protect Sogroya® from direct light. See figure T.

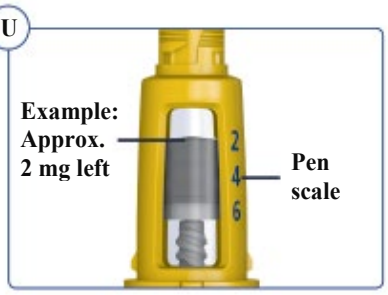
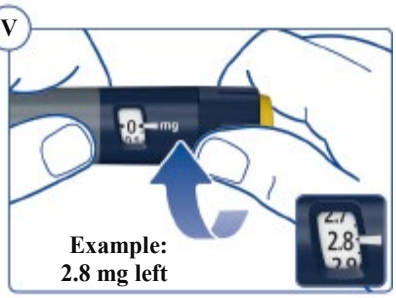
  To store your pen, see *'Storage'* in the *Patient Medication Information.*



⚠ **Do not try to put the inner needle cap back on.**
You may stick yourself with the needle.

⚠ Always remove the needle from your pen immediately after each injection. This reduces the risk of contamination, infection, leakage of Sogroya®, and blocked needles leading to incorrect dosing.

Frequently Asked Questions

How do I see how much Sogroya® is left in my pen? The pen scale shows you approximately how much Sogroya® is left in your pen. See figure U.	U 
To see how much Sogroya® is left, use the dose counter: Turn the dose selector clockwise until the dose counter stops. You can select a maximum dose of 4 mg. If it shows "4", at least 4 mg are left in your pen. If the dose counter stops at "2.8", only 2.8 mg are left in your pen. See figure V.	V 

What if I need a larger dose than what is left in my pen?	It is not possible to select a larger dose than the amount of mg left in your pen. If you need more Sogroya® than you have left in your pen, you can use a new pen or split your dose between your current pen and a new pen. **Only if trained or advised by your doctor or nurse, may you split your dose.** Use a calculator to plan the doses as instructed by your doctor or nurse. **Be very careful to calculate correctly, otherwise it may lead to medication error.** If you are not sure how to split your dose using two pens, then select and inject the dose you need with a new pen.
What if no Sogroya® appears when I check the flow?	**A. Your needle may be blocked or damaged,** if no Sogroya® appears at the needle tip. Remove the needle as described in step 5 and repeat steps 1 and 2. **B. Your pen may be defective,** if Sogroya® still does not appear after changing the needle. Do not use the pen.
What if "0" does not appear after completing my injection?	In this case the needle or pen may be blocked or damaged, and **you have not received any Sogroya®** – even though the dose counter has moved from the original dose that you have set. Remove the needle as described in step 5 and repeat steps 1 to 4.
How should I take care of my pen?	Be careful not to drop your pen or knock it against hard surfaces. Do not expose your pen to dust, dirt, liquid, or direct light. If there is Sogroya® left in the pen, store the pen as directed in *'Storage'* in the *Patient Medication Information.* Do not try to refill your pen, it is prefilled and must be disposed of when empty.

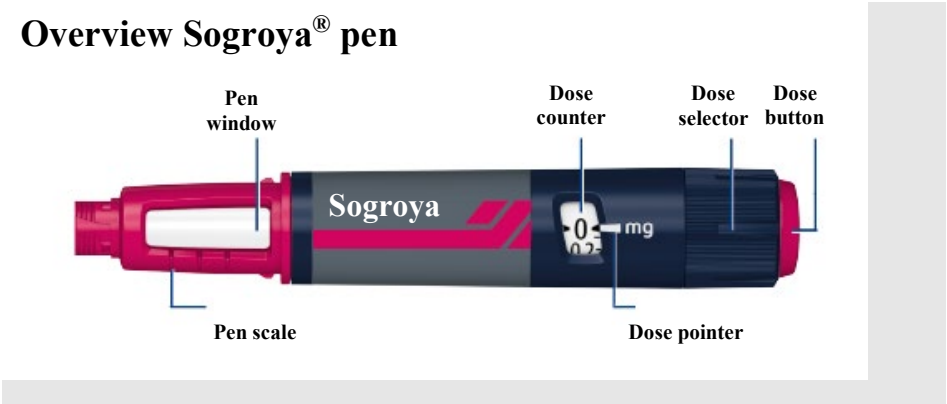
What if I drop my pen?	If you drop your pen or think that something is wrong with it, attach a new disposable needle and check the flow before you inject, see steps 1 and 2. If your pen has been dropped, check the cartridge, if the cartridge is cracked, do not use the pen. Do not try to repair your pen or pull it apart.
How do I clean my pen?	Do not wash, soak, or lubricate your pen. It may be cleaned with a mild detergent on a moistened cloth.

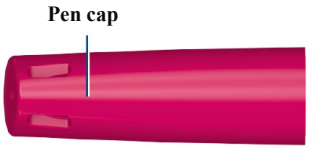
 **Important information**

- Caregivers must be very careful when handling needles – to reduce the risk of needle sticks and cross-infection.
- Always keep your pen and needles out of reach of others, especially children.
- **Do not use the pen** if it is damaged. Do not try to repair your pen or pull it apart.
- To store your pen, *see 'Storage'* in the *Patient Medication Information.*

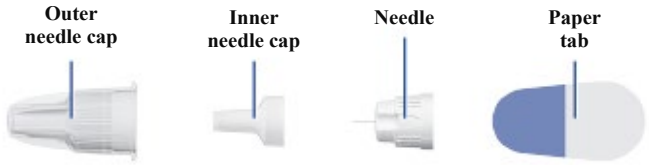
Instructions For Use

Overview Sogroya® pen





Needle (example)



How to use your once weekly Sogroya® pen

5 steps you should follow for a Sogroya® injection:

Step 1. Prepare your Sogroya® pen

Step 2. Check the flow with each new pen

Step 3. Select your dose

Step 4. Inject your dose

Step 5. After your injection

For further information about your pen: see sections *Frequently Asked Questions, Important information, Patient Information*
Please read these instructions carefully before using your Sogroya® prefilled pen.

⚠ Pay special attention to these notes as they are important for safe use of the pen.

ⓘ Additional information

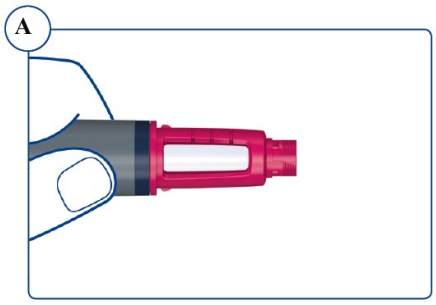
Sogroya® is a prefilled growth hormone pen. It contains 15 mg of Sogroya® and delivers doses from 0.1 mg to 8 mg, in increments of 0.1 mg. Sogroya® is for use under the skin only (subcutaneous). Sogroya® prefilled pen is designed to be used with NovoFine® disposable needles up to a length of 8 mm.

Do not share your Sogroya® pen and needles with another person. You may give another person an infection or get an infection from them.

Do not use your pen without proper training from your doctor or nurse. Make sure that you are confident in making an injection with the pen before you start your treatment. If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help. Get help from a person with good eyesight who is trained to use the pen.

Step 1. Prepare your once weekly Sogroya® pen

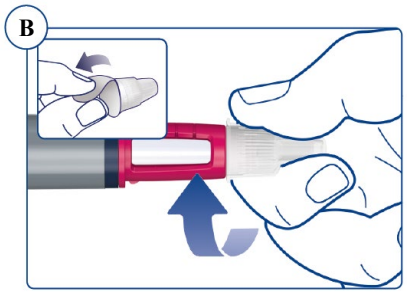
- Wash your hands with soap and water.
- **Check the name, strength, and coloured label** on your pen to make sure that it contains Sogroya® in the right strength.
- Pull off the pen cap.
- Turn the pen upside down once or twice to check that the Sogroya® in your pen is clear and colourless. See figure A. **If the Sogroya® looks cloudy, do not use the pen.**



⚠ Make sure the right pen is used. Especially if you use more than one type of injectable medicine. Using the wrong medicine could be harmful to your health.

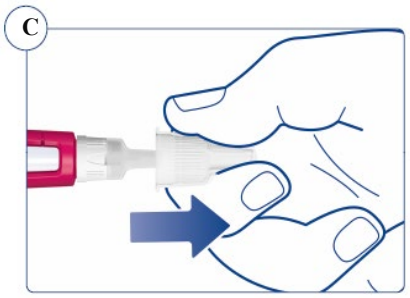
When you are ready to take your injection

- Firstly, take a new disposable needle and tear off the paper tab.
- Then push the needle straight onto the pen. Turn the needle clockwise **until it is on tight.** See figure B.



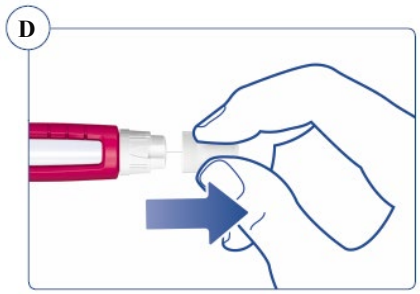
- Pull off the outer needle cap and keep it for later. You will need it after the injection, to safely remove the needle from the pen. See figure C.

ⓘ The needle is covered by two caps. You must remove both caps. If you forget to remove both caps you will not inject any medicine.



- Pull off the inner needle cap and dispose of it. If you try to put it back on, you may accidentally stick yourself with the needle. See figure D.

ⓘ A drop of Sogroya® may appear at the needle tip. This is normal, but you must still check the flow with each new pen. See step 2.



⚠ **Always use a new needle for each injection.** This reduces the risk of contamination, infection, leakage of Sogroya®, and blocked needles leading to incorrect dosing.

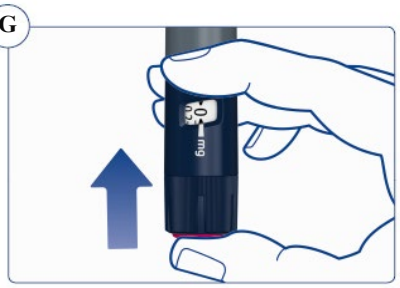
⚠ Never use a bent or damaged needle.

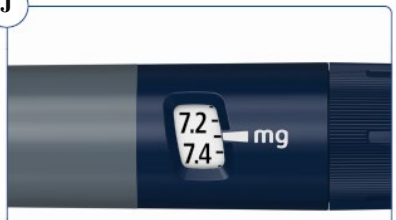
Step 2. Check the flow with each new pen

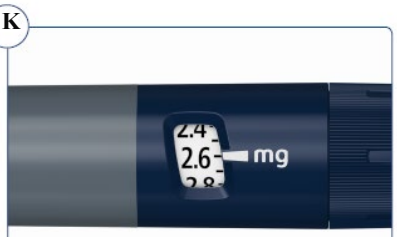
ⓘ **If your pen is already in use,** proceed to step 3.

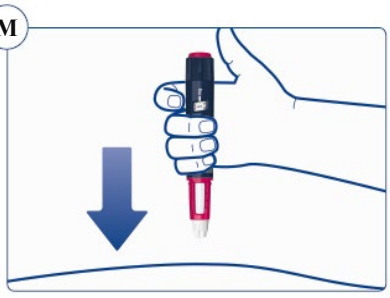
- **Before using a new pen,** check the flow to make sure Sogroya® can flow through the pen and needle.
- Turn the dose selector clockwise one tick mark to select 0.1 mg. You may hear a faint click. See figure E.

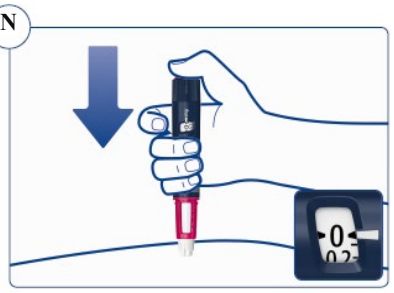
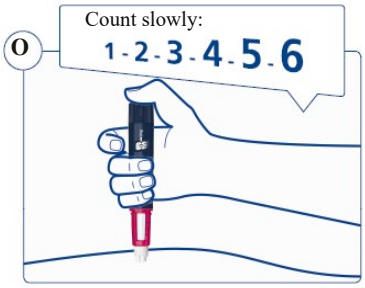
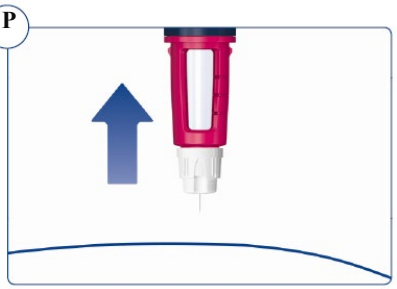
- **One tick mark equals 0.1 mg** in the dose counter. See figure F.

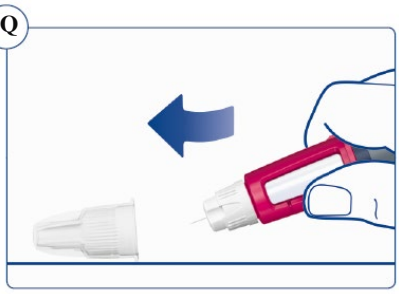
• Hold the pen with the needle pointing up. Press and hold in the dose button until the dose counter returns to "0". **The "0" must line up with the dose pointer.** See figure G.	G 
• Check that a drop of Sogroya® appears at the needle tip. See figure H. ⓘ **If no Sogroya® appears,** repeat step 2 up to 6 times. If you still do not see a drop of Sogroya®, **change the needle.** Remove the needle as described in step 5 and repeat step 1 and 2 again. **Do not use the pen if a drop of Sogroya® still does not appear after repeating step 2.**	H 

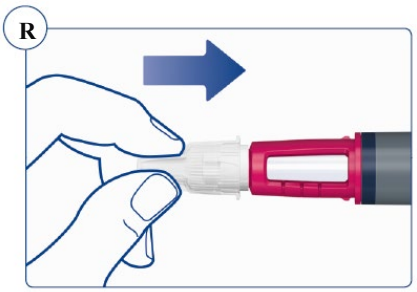
Step 3. Select your dose	
• To start, check that the dose counter is set at "**0".** • Turn the dose selector clockwise to select the dose you need. See figure I. When you have selected your dose, you can proceed to step 4. ⓘ **If there is not enough Sogroya® left** to select a full dose, *see Frequently Asked Questions.*	I 
ⓘ The dose counter shows the dose in mg. See figures J and K. Always use the dose pointer to select the exact dose. **Do not count the pen clicks. Do not use the pen scale.**	J  **Example: 7.3 mg selected**

	K  **Example: 2.6 mg selected**
ⓘ If you select the wrong dose, you can turn the dose selector clockwise or counterclockwise to the correct dose. See figure L. The pen clicks sound and feel differently when the dose selector is turned clockwise, counterclockwise, or if you accidentally force it past the number of mg left.	L 

Step 4. Inject your dose	
• Insert the needle into your skin as your doctor or nurse has shown you. See figure M. Make sure you can see the dose counter. **Do not cover it with your fingers.** This could block the injection. ⓘ **Remember to change the injection site every week.**	M 
• **Press and hold down the dose button until the dose counter shows "0". Keep pressing the dose button with the needle in your skin and slowly count to 6**. See figure N and O. The "0" must line up with the dose pointer. You may then hear or feel a click. ⓘ If "0" does not appear in the dose counter after continuously pressing the dose button, your needle or pen may be blocked or damaged, see *Frequently Asked Questions.*	

	N  O 
• Carefully remove the needle from your skin. See figure P. If blood appears at the injection site, press lightly. Do not rub the area. ⓘ You may see a drop of Sogroya® at the needle tip after injecting. This is normal and does not affect your dose.	P 

Step 5. After your injection	
• Insert the needle tip into the outer needle cap on a flat surface without touching the needle or the outer needle cap. See figure Q.	Q 
• Once the needle is covered, carefully push the outer needle cap completely on. See figure R.	



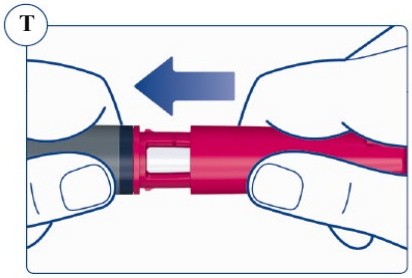
- Unscrew the needle and dispose of it carefully as instructed by your doctor, nurse, pharmacist or local authorities.

  Always dispose of the needle after each injection.
  When the pen is empty, throw it away **without** a needle on as instructed by your doctor, nurse, pharmacist or local authorities.

  The pen cap and the empty carton can be disposed of in your household trash.

- Put the pen cap on your pen after each use to protect Sogroya® from direct light. See figure T.

  To store your pen, see *'Storage'* in the *Patient Medication Information.*



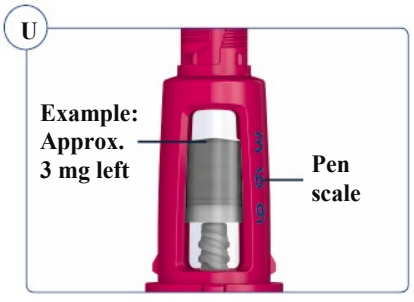
⚠ **Do not try to put the inner needle cap back on.**
You may stick yourself with the needle.

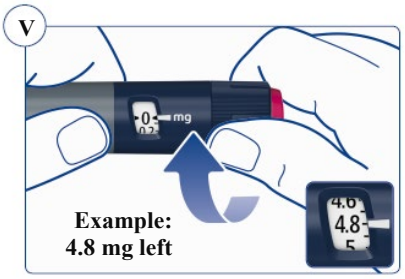
⚠ Always remove the needle from your pen immediately after each injection. This reduces the risk of contamination, infection, leakage of Sogroya®, and blocked needles leading to incorrect dosing.

Frequently Asked Questions

How do I see how much Sogroya® is left in my pen?

The pen scale shows you approximately how much Sogroya® is left in your pen. See figure U.



To see how much Sogroya® is left, use the dose counter: Turn the dose selector clockwise until the dose counter stops. You can select a maximum dose of 8 mg. If it shows "8", at least 8 mg are left in your pen. If the dose counter stops at "4.8", only 4.8 mg are left in your pen. See figure V.	
What if I need a larger dose than what is left in my pen?	It is not possible to select a larger dose than the amount of mg left in your pen. If you need more Sogroya® than you have left in your pen, you can use a new pen or split your dose between your current pen and a new pen. **Only if trained or advised by your doctor or nurse, may you split your dose.** Use a calculator to plan the doses as instructed by your doctor or nurse. **Be very careful to calculate correctly, otherwise it may lead to medication error.** If you are not sure how to split your dose using two pens, then select and inject the dose you need with a new pen.
What if no Sogroya® appears when I check the flow?	**A. Your needle may be blocked or damaged,** if no Sogroya® appears at the needle tip. Remove the needle as described in step 5 and repeat steps 1 and 2. **B. Your pen may be defective,** if Sogroya® still does not appear after changing the needle. Do not use the pen.
What if "0" does not appear after completing my injection?	In this case the needle or pen may be blocked or damaged, and **you have not received any Sogroya®** – even though the dose counter has moved from the original dose that you have set. Remove the needle as described in step 5 and repeat steps 1 to 4.
How should I take care of my pen?	Be careful not to drop your pen or knock it against hard surfaces. Do not expose your pen to dust, dirt, liquid, or direct light. If there is Sogroya® left in the pen, store the pen as directed in *'Storage'* in the *Patient Medication Information.* Do not try to refill your pen, it is prefilled and must be disposed of when empty.
What if I drop my pen?	If you drop your pen or think that something is wrong with it, attach a new disposable needle and check the flow before you inject, see steps 1 and 2. If your pen has been dropped, check the cartridge, if the cartridge is cracked, do not use the pen. Do not try to repair your pen or pull it apart.
How do I clean my pen?	Do not wash, soak, or lubricate your pen. It may be cleaned with a mild detergent on a moistened cloth.

Important information

- Caregivers must be very careful when handling needles – to reduce the risk of needle sticks and cross-infection.
- Always keep your pen and needles out of reach of others, especially children.
- **Do not use the pen** if it is damaged. Do not try to repair your pen or pull it apart.
- To store your pen, *see 'Storage'* in the *Patient Medication Information.*