

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use SKYTROFA™ safely and effectively. See full prescribing information for SKYTROFA™.

**SKYTROFA™ (lonapegsomatropin-tcgd) for injection, for subcutaneous use**

**Initial U.S. Approval: 2021**

### -----INDICATIONS AND USAGE-----

SKYTROFA is a human growth hormone indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH) (1).

### -----DOSAGE AND ADMINISTRATION-----

SKYTROFA should be administered subcutaneously into the abdomen, buttock, or thigh with regular rotation of the injection sites (2.5). The recommended dose is 0.24 mg/kg body weight once-weekly.

See Full Prescribing Information for instructions on preparation and administration of drug (2.4, 2.5).

### -----DOSAGE FORMS AND STRENGTHS-----

SKYTROFA is a lyophilized powder available in single-dose, dual-chamber, prefilled cartridges containing lonapegsomatropin-tcgd and diluent, Water for Injection, as follows:

For injection: 3 mg, 3.6 mg, 4.3 mg, 5.2 mg, 6.3 mg, 7.6 mg, 9.1 mg, 11 mg and 13.3 mg (3).

### -----CONTRAINDICATIONS-----

- Acute critical illness (4)
- Hypersensitivity to somatropin or any of the excipients in SKYTROFA (4)
- Children with closed epiphyses (4)
- Active malignancy (4)
- Active proliferative or severe non-proliferative diabetic retinopathy (4)
- Children with Prader-Willi syndrome who are severely obese or have severe respiratory impairment due to risk of sudden death (4)

### -----WARNINGS AND PRECAUTIONS-----

- Severe Hypersensitivity: Serious hypersensitivity reactions may occur. In the event of an allergic reaction, seek prompt medical attention (5.2).
- Increased Risk of Neoplasms: Monitor patients with preexisting tumors for progressions or recurrence. Increased risk of a second neoplasm in childhood cancer survivors treated with somatropin – in particular meningiomas in patients treated with radiation to the head for their first neoplasm (5.3).

- Glucose Intolerance and Diabetes Mellitus: May be unmasked. Periodically monitor glucose levels in all patients. Doses of concurrent antihyperglycemic drugs in diabetics may require adjustment (5.4).
- Intracranial Hypertension: Exclude preexisting papilledema. May develop and is usually reversible after discontinuation or dose reduction (5.5).
- Fluid Retention (i.e., edema, arthralgia, carpal tunnel syndrome): May occur. Reduce dose as necessary (5.6).
- Hypoadrenalism: Monitor patients for reduced serum cortisol levels and/or need for glucocorticoid dose increases in those with known hypoadrenalism (5.7).
- Hypothyroidism: May first become evident or worsen (5.8).
- Slipped Capital Femoral Epiphysis: May develop. Evaluate children with the onset of a limp or persistent hip/knee pain (5.9).
- Progression of Preexisting Scoliosis: May develop (5.10).
- Pancreatitis: Consider pancreatitis in patients with persistent severe abdominal pain (5.11).

### -----ADVERSE REACTIONS-----

Most common adverse reactions (≥5%) in pediatric patients include: viral infection, pyrexia, cough, nausea and vomiting, hemorrhage, diarrhea, abdominal pain, and arthralgia and arthritis (6).

**To report SUSPECTED ADVERSE REACTIONS, contact Ascendis Pharma, Inc., at 1-844-442-7236 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

### -----DRUG INTERACTIONS-----

- Replacement Glucocorticoid Treatment: Patients treated with glucocorticoid for hypoadrenalism may require an increase in their maintenance or stress doses following initiation of SKYTROFA (7).
- Pharmacologic Glucocorticoid Therapy and Supraphysiologic Glucocorticoid Treatment: Adjust glucocorticoid replacement dosing in pediatric patients receiving glucocorticoid treatment to avoid both hypoadrenalism and an inhibitory effect on growth (7).
- Cytochrome P450-Metabolized Drugs: SKYTROFA may alter the clearance. Monitor carefully if used with SKYTROFA (7).
- Oral Estrogen: Larger doses of SKYTROFA may be required (7).
- Insulin and/or Other Antihyperglycemic Agents: Dose adjustment of insulin or antihyperglycemic agent may be required (7).

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

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## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

SKYTROFA (lonapegsomatropin-tcgd) is a human growth hormone indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH).

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 General Dosing Information

- For subcutaneous injection, once-weekly.
- Therapy with SKYTROFA should be supervised by a physician who is experienced in the diagnosis and management of pediatric patients with growth failure due to growth hormone deficiency (GHD).
- To exclude preexisting papilledema, perform fundoscopic examination before initiating treatment with SKYTROFA and reassess periodically thereafter [*see Warnings and Precautions (5.5)*].

#### 2.2 Dosage Recommendations

- The recommended dose of SKYTROFA for treatment-naïve patients and patients switching from daily somatropin therapy is 0.24 mg/kg body weight, given once-weekly.
- Individualize and titrate the dosage of SKYTROFA based on response.
- When changing from daily somatropin therapy to once-weekly SKYTROFA, wait at least 8 hours between the final dose of daily somatropin and the first dose of once-weekly SKYTROFA.
- Assess compliance and evaluate other causes of poor growth such as hypothyroidism, under-nutrition, advanced bone age and antibodies to recombinant human growth hormone if patients experience failure to increase height velocity, particularly during the first year of treatment.
- Discontinue SKYTROFA once epiphyseal fusion has occurred.

#### 2.3 Missed Doses

- Administer a missed dose as soon as possible and not more than 2 days after the missed dose.
- To avoid missed doses, SKYTROFA can be taken 2 days before or 2 days after the scheduled dosing day. Resume once-weekly dosing for the next dose at the previously scheduled dosing day.
- If more than 2 days have passed from the scheduled day, skip the dose and administer the next dose on the regularly scheduled day.
- At least 5 days should elapse between doses.

## 2.4 Administration Instructions

SKYTROFA is available in 9 cartridges (dosage strengths in somatotropin equivalents). Selection of the appropriate cartridge is based on the prescribed dose (mg/kg) and the patient's body weight (kg).

- If prescribing a dose of 0.24 mg/kg/week and the patient's weight is 11.5 to 100 kg, follow the recommended dosing in [Table 1](#).
- If prescribing a dose other than 0.24 mg/kg/week, calculate the total weekly dose (in mg) and select the appropriate cartridge as follows:
  - Total weekly dose (mg) = prescribed weekly dose (mg/kg) x patient's body weight (kg).
  - Round the total weekly dose (mg) to the closest cartridge dose while also considering treatment goals and clinical response.

**Table 1: Recommended Dosing for Patients Prescribed Doses of 0.24 mg/kg/week**

Weight (kg)	Dose (mg)
11.5 – 13.9	3
14 – 16.4	3.6
16.5 – 19.9	4.3
20 – 23.9	5.2
24 – 28.9	6.3
29 – 34.9	7.6
35 – 41.9	9.1
42 – 50.9	11
51 – 60.4	13.3
60.5 – 69.9	15.2 (using two cartridges of 7.6 mg each)
70 – 84.9	18.2 (using two cartridges of 9.1 mg each)
85 – 100	22 (using two cartridges of 11 mg each)

## 2.5 Preparation and Administration

- The SKYTROFA cartridge has been designed for use only with the SKYTROFA Auto-Injector.
- If refrigerated, the SKYTROFA cartridge must be kept at room temperature for 15 minutes before use.
- The SKYTROFA Auto-Injector provides a fully automated reconstitution of the lyophilized drug product which is followed by a manual mixing step controlled by the device. When the injection needle is inserted into the skin, the device automatically delivers the drug product. The built-in electronics and software assist the user during the entire preparation and injection sequence and provide confirmation that the full dose has been delivered.

- The mixed solution should be clear and colorless to opalescent and may occasionally contain air bubbles. DO NOT inject if the solution is cloudy or contains particulate matter.
- Use SKYTROFA cartridges within 4 hours after reconstitution. Discard reconstituted SKYTROFA cartridges after 4 hours when stored at room temperature up to 86°F (30°C).
- Inject SKYTROFA subcutaneously into the abdomen, buttock, or thigh. Rotate injection sites between and within regions to reduce the risk of lipoatrophy.
- Refer to the Instructions for Use for complete administration instructions with illustrations. The instructions can also be found on [www.Skytrofa.com/IFU](http://www.Skytrofa.com/IFU).

### 3 DOSAGE FORMS AND STRENGTHS

SKYTROFA is a white to off-white lyophilized powder available in a single-dose, dual-chamber, prefilled cartridge containing lonapegsomatropin-tcgd in one chamber and diluent, Water for Injection, in the other chamber and is available in the following strengths:

For injection: 3 mg, 3.6 mg, 4.3 mg, 5.2 mg, 6.3 mg, 7.6 mg, 9.1 mg, 11 mg and 13.3 mg.

### 4 CONTRAINDICATIONS

SKYTROFA is contraindicated in patients with:

- Acute critical illness after open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure due to the risk of increased mortality with use of pharmacologic doses of somatropin [*see Warnings and Precautions (5.1)*].
- Hypersensitivity to somatropin or any of the excipients in SKYTROFA. Systemic hypersensitivity reactions have been reported with post-marketing use of somatropin products [*see Warnings and Precautions (5.2)*].
- Closed epiphyses.
- Active malignancy due to the risk of malignancy progression [*see Warnings and Precautions (5.3)*].
- Active proliferative or severe non-proliferative diabetic retinopathy because treatment with somatropin may worsen this condition.
- Prader-Willi syndrome who are severely obese, have a history of upper airway obstruction or sleep apnea or have severe respiratory impairment due to the risk of sudden death [*see Warnings and Precautions (5.13)*].

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Increased Mortality in Patients with Acute Critical Illness

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 has been reported after treatment with pharmacologic doses of somatropin [*see Contraindications (4)*]. The safety of continuing SKYTROFA treatment in patients receiving

replacement doses for the approved indication who concurrently develop these illnesses has not been established.

## 5.2 Severe Hypersensitivity

Serious systemic hypersensitivity reactions including anaphylactic reactions and angioedema have been reported with post-marketing use of somatropin products. Inform patients and caregivers that such reactions are possible, and that prompt medical attention should be sought if an allergic reaction occurs [see *Contraindications (4)*]. Do not use SKYTROFA in patients with known hypersensitivity to somatropin or any of the excipients in SKYTROFA.

## 5.3 Increased Risk of Neoplasms

### *Active Malignancy*

There is an increased risk of malignancy progression with somatropin treatment in patients with active malignancy [see *Contraindications (4)*]. Any preexisting malignancy should be inactive, and its treatment should be completed prior to instituting therapy with SKYTROFA. Discontinue SKYTROFA if there is evidence of recurrent malignancy.

### *Risk of Second Neoplasm in Pediatric Patients*

In childhood cancer survivors who were treated with radiation to the brain/head for their first neoplasm and who developed subsequent growth hormone deficiency (GHD) and were treated with somatropin, an increased risk of a second neoplasm has been reported. Intracranial tumors, in particular meningiomas, were the most common of these second neoplasms. Monitor all patients with a history of GHD secondary to an intracranial neoplasm while on somatropin therapy for progression or recurrence of the tumor.

### *New Malignancy During Treatment*

Because children with certain rare genetic causes of short stature have an increased risk of developing malignancies, thoroughly consider the risks and benefits of starting somatropin in these patients. If treatment with somatropin is initiated, carefully monitor these patients for development of neoplasms.

Monitor patients on somatropin therapy carefully for increased growth or potential malignant changes of preexisting nevi. Advise patients/caregivers to report marked changes in behavior, onset of headaches, vision disturbances and/or changes in skin pigmentation or changes in the appearance of preexisting nevi.

## 5.4 Glucose Intolerance and Diabetes Mellitus

Treatment with somatropin may decrease insulin sensitivity, particularly at higher doses. Previously undiagnosed impaired glucose tolerance and overt type 2 diabetes mellitus may be unmasked. Monitor glucose levels in all patients receiving SKYTROFA, especially in those with risk factors for type 2 diabetes mellitus, such as obesity or a family history of type 2 diabetes mellitus. When initiating SKYTROFA, monitor closely patients with preexisting type 1 or type 2 diabetes mellitus or impaired glucose tolerance and adjust the doses of antihyperglycemic drugs as needed.

### **5.5 Intracranial Hypertension**

Intracranial hypertension (IH) with papilledema, visual changes, headache, nausea, and/or vomiting has been reported in a small number of patients treated with somatropin. Symptoms usually occurred within 8 weeks after the initiation of somatropin. In all reported cases, IH-associated signs and symptoms resolved rapidly after cessation of therapy or a reduction of the somatropin dose. To exclude preexisting papilledema, perform fundoscopic examination before initiating treatment with SKYTROFA, and reassess periodically thereafter. If papilledema is observed by fundoscopy, stop somatropin treatment. If somatropin-induced IH is confirmed, restart treatment with SKYTROFA at a lower dose after IH-associated signs and symptoms have resolved.

### **5.6 Fluid Retention**

Fluid retention during somatropin therapy may occur. Clinical manifestations of fluid retention (e.g., edema, arthralgia, myalgia, nerve compression syndromes including carpal tunnel syndrome/paresthesia) are usually transient and dose-dependent.

### **5.7 Hypoadrenalism**

Patients receiving somatropin therapy who have or are at risk for pituitary hormone deficiency(s) may be at risk for reduced serum cortisol levels and/or unmasking of central (secondary) hypoadrenalism. In addition, patients treated with glucocorticoid replacement for previously diagnosed hypoadrenalism may require an increase in their maintenance or stress doses following initiation of SKYTROFA therapy. Monitor patients for reduced serum cortisol levels and/or need for glucocorticoid dose increases in patients with known hypoadrenalism [*see Drug Interactions (7)*].

### **5.8 Hypothyroidism**

Undiagnosed or untreated hypothyroidism may prevent optimal response to SKYTROFA. In patients with GHD, central (secondary) hypothyroidism may first become evident or worsen during SKYTROFA treatment. Therefore, perform periodic thyroid function tests in patients and initiate or appropriately adjust thyroid hormone replacement therapy when indicated.

### **5.9 Slipped Capital Femoral Epiphysis**

Slipped capital femoral epiphysis may occur more frequently in patients undergoing rapid growth. Evaluate pediatric patients with the onset of a limp or complaints of persistent hip or knee pain.

### **5.10 Progression of Preexisting Scoliosis**

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

### 5.11 Pancreatitis

Pancreatitis has been reported in pediatric patients receiving somatropin. The risk may be greater in pediatric patients than adults. Consider pancreatitis in patients who develop persistent severe abdominal pain.

### 5.12 Lipoatrophy

When SKYTROFA is administered subcutaneously at the same site over a long period of time, lipoatrophy may result. Rotate injection sites when administering SKYTROFA to reduce this risk [*see Preparation and Administration (2.5)*].

### 5.13 Sudden Death in Pediatric 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. Male patients with one or more of these factors may be at greater risk than females. SKYTROFA is not indicated for the treatment of pediatric patients who have growth failure due to genetically confirmed Prader-Willi syndrome.

### 5.14 Laboratory Tests

Serum levels of phosphate, alkaline phosphatase, and parathyroid hormone may increase after somatropin treatment. If a patient is found to have abnormal laboratory tests, monitor as appropriate.

## 6 ADVERSE REACTIONS

The following important adverse reactions are described elsewhere in the labeling:

- Increased mortality in patients with acute critical illness [*see Warnings and Precautions (5.1)*]
  - Severe hypersensitivity [*see Warnings and Precautions (5.2)*]
  - Increased risk of neoplasms [*see Warnings and Precautions (5.3)*]
  - Glucose intolerance and diabetes mellitus [*see Warnings and Precautions (5.4)*]
  - Intracranial hypertension [*see Warnings and Precautions (5.5)*]
  - Fluid retention [*see Warnings and Precautions (5.6)*]
  - Hypoadrenalism [*see Warnings and Precautions (5.7)*]
  - Hypothyroidism [*see Warnings and Precautions (5.8)*]
  - Slipped capital femoral epiphysis in pediatric patients [*see Warnings and Precautions (5.9)*]
  - Progression of preexisting scoliosis in pediatric patients [*see Warnings and Precautions (5.10)*]
  - Pancreatitis [*see Warnings and Precautions (5.11)*]
  - Lipoatrophy [*see Warnings and Precautions (5.12)*]
-

- Sudden death in pediatric patients with Prader-Willi syndrome [see *Warnings and Precautions (5.13)*]

## 6.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in clinical practice.

SKYTROFA was studied in a 52-week, open-label, active-controlled trial in 161 treatment-naïve, prepubertal pediatric patients with growth hormone deficiency (GHD) [see *Clinical Studies (14.1)*]. The subjects ranged in age from 3.2 to 13.1 years with a mean of 8.5 years. One hundred thirty-two (82%) of the subjects were male and 29 (18%) were female. One subject was Asian, 3 were Black or African American, 152 were Caucasian, and 5 were categorized as “other.”

Table 2 shows common adverse reactions that occurred in  $\geq 5\%$  of patients treated with SKYTROFA in this trial.

**Table 2: Adverse Reactions Occurring in  $\geq 5\%$  SKYTROFA-Treated Pediatric Patients and More Frequently than in Daily Somatotropin-Treated Pediatric Patients (52 Weeks of Treatment)**

Adverse Reactions	Daily Somatotropin (N = 56) n (%)	SKYTROFA (N = 105) n (%)
Infection, viral	6 (11%)	16 (15%)
Pyrexia	5 (9%)	16 (15%)
Cough	4 (7%)	11 (11%)
Nausea and vomiting	4 (7%)	11 (11%)
Hemorrhage <sup>a</sup>	1 (2%)	7 (7%)
Diarrhea	3 (5%)	6 (6%)
Abdominal pain	2 (4%)	6 (6%)
Arthralgia and arthritis <sup>b</sup>	1 (2%)	6 (6%)

Adverse reactions that are medically related were grouped to a single preferred term.

<sup>a</sup> Hemorrhage in the SKYTROFA treatment group included epistaxis (3), contusion (2), petechiae (1) and eye hemorrhage (1).

<sup>b</sup> Arthralgia and arthritis in the SKYTROFA treatment group included arthralgia (5) and reactive arthritis (1).

### Laboratory Tests

More SKYTROFA-treated patients shifted from normal baseline levels to elevated phosphate and alkaline phosphatase levels at the end of the trial compared to the daily somatotropin group (44.2% vs. 30.2% and 19.2% vs. 9.4%, respectively); these laboratory changes occurred intermittently [see *Warnings and Precautions (5.14)*].

## 6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to SKYTROFA with the incidence of antibodies to other products may be misleading.

Anti-lonapegsomatropin-tcgd antibodies were evaluated in samples collected every 3 months in phase 3 trials in pediatric patients with GHD receiving lonapegsomatropin-tcgd. Mean duration of exposure to SKYTROFA was 70.2 weeks. Of the 304 patients with post-baseline assessments, 19 (6.3%) showed detectable binding antibodies to lonapegsomatropin-tcgd at any time. No apparent correlation of anti-lonapegsomatropin-tcgd antibodies to adverse events or loss of efficacy was observed. No neutralizing antibodies to SKYTROFA were detected.

## 7 DRUG INTERACTIONS

Table 3 includes a list of drugs with clinically important drug interactions when administered concomitantly with SKYTROFA and instructions for preventing or managing them.

**Table 3: Clinically Important Drug Interactions with SKYTROFA**

<b>Replacement Glucocorticoid Treatment</b>	
<i>Clinical Impact:</i>	Microsomal enzyme 11 $\beta$ -hydroxysteroid dehydrogenase type 1 (11 $\beta$ HSD-1) is required for conversion of cortisone to its active metabolite, cortisol, in hepatic and adipose tissue. Somatropin inhibits 11 $\beta$ HSD-1. Consequently, individuals with untreated growth hormone deficiency (GHD) have relative increases in 11 $\beta$ HSD-1 and serum cortisol. Initiation of SKYTROFA may result in inhibition of 11 $\beta$ HSD-1 and reduced serum cortisol concentrations.
<i>Intervention:</i>	Patients treated with glucocorticoid replacement for hypoadrenalism may require an increase in their maintenance or stress doses following initiation of SKYTROFA [ <i>see Warnings and Precautions (5.7)</i> ]
<i>Examples</i>	Cortisone acetate and prednisone may be affected more than others because conversion of these drugs to their biologically active metabolites is dependent on the activity of 11 $\beta$ HSD-1.
<b>Pharmacologic Glucocorticoid Therapy and Supraphysiologic Glucocorticoid Treatment</b>	
<i>Clinical Impact:</i>	Pharmacologic glucocorticoid therapy and supraphysiologic glucocorticoid treatment may attenuate the growth-promoting effects of SKYTROFA in pediatric patients.
<i>Intervention:</i>	Carefully adjust glucocorticoid replacement dosing in pediatric patients receiving glucocorticoid treatments to avoid both hypoadrenalism and an inhibitory effect on growth.
<b>Cytochrome P450-Metabolized Drugs</b>	

<i>Clinical Impact:</i>	Limited published data indicate that somatropin treatment increases cytochrome P450 (CYP450)-mediated antipyrine clearance. SKYTROFA may alter the clearance of compounds known to be metabolized by CYP450 liver enzymes.
<i>Intervention:</i>	Careful monitoring is advisable when SKYTROFA is administered in combination with drugs metabolized by CYP450 liver enzymes.
<b>Oral Estrogen</b>	
<i>Clinical Impact:</i>	Oral estrogens may reduce the serum insulin-like growth factor-1 (IGF-1) response to SKYTROFA.
<i>Intervention:</i>	Patients receiving oral estrogen replacement may require higher SKYTROFA dosages.
<b>Insulin and/or Other Antihyperglycemic Agents</b>	
<i>Clinical Impact:</i>	Treatment with SKYTROFA may decrease insulin sensitivity, particularly at higher doses.
<i>Intervention:</i>	Patients with diabetes mellitus may require adjustment of their doses of insulin and/or other antihyperglycemic agents [ <i>see Warnings and Precautions (5.4)</i> ].

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

#### Risk Summary

There are no available data on lonapegsomatropin-tcgd use in pregnant patients to evaluate a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Available published data over several decades for somatropin, the active component of lonapegsomatropin-tcgd, have not identified a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. In animal reproduction studies, there was no evidence of embryo-fetal or neonatal harm when pregnant rats were administered subcutaneous lonapegsomatropin-tcgd at doses up to 13-fold the clinical dose of 0.24 mg/kg/week (*see Data*).

The estimated background risk of birth defects and miscarriages for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriages in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

#### Data

##### *Animal Data*

No embryonic or fetal development toxicities occurred in rats administered subcutaneous lonapegsomatropin-tcgd at doses up to 13-fold the clinical dose of 0.24 mg/kg/week.

In a peri- and post-natal developmental study in rats, there were no adverse effects on the pregnant/lactating female or on development of the conceptus and the offspring following exposure of the female from implantation through weaning to doses of a structurally related pegylated somatropin prodrug up to 13-fold the clinical dose of 0.24 mg/kg/week.

## 8.2 Lactation

### Risk Summary

There are no data on the presence of lonapegsomatropin-tcgd in human milk, effects on the breastfed infant, or effects on milk production. High molecular weight therapeutic proteins, including lonapegsomatropin-tcgd, are expected to have low passage into human milk and limited systemic exposure in the breastfed infant. Additionally, published data indicate that exogenous somatropin does not increase normal human milk concentrations of growth hormone. No adverse effects on the breastfed infant have been reported with somatropin. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for SKYTROFA and any potential adverse effects on the breastfed infant from SKYTROFA or from the underlying maternal condition.

## 8.4 Pediatric Use

Safety and effectiveness of SKYTROFA have been established in pediatric patients 1 year and older and who weigh at least 11.5 kg. Pediatric use was established in a controlled study of 161 treatment-naïve pediatric patients ages 3 to 13 years and by supportive data in pediatric patients 1 year and older [*see Adverse Reactions (6) and Clinical Studies (14)*].

The safety and effectiveness of SKYTROFA in children less than 1 year of age have not been established.

Use of somatropin in pediatric patients with Prader-Willi syndrome has been associated with reports of sudden death. SKYTROFA is not indicated for the treatment of pediatric patients with growth failure due to genetically confirmed Prader-Willi syndrome [*see Warnings and Precautions (5.13)*].

## 9 DRUG ABUSE AND DEPENDENCE

### 9.1 Controlled Substance

SKYTROFA is a prodrug of somatropin. Somatropin is not a controlled substance.

### 9.2 Abuse

Inappropriate use of somatropin may result in significant negative health consequences.

### 9.3 Dependence

Somatropin is not associated with drug related withdrawal adverse reactions.

## 10 OVERDOSAGE

Acute overdosage may lead initially to hypoglycemia and subsequently to hyperglycemia. Overdose with somatropin may cause fluid retention. Long-term overdosage may result in signs and symptoms of gigantism consistent with the known effects of excess growth hormone.

## 11 DESCRIPTION

Lonapegsomatropin-tcgd is a long-acting prodrug of a human growth hormone (somatropin) produced by recombinant DNA technology using *E. coli*. Lonapegsomatropin-tcgd consists of a

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parent drug, somatotropin, that is conjugated to a methoxypolyethylene glycol carrier (4 x 10 kDa mPEG) via a proprietary TransCon Linker and has a molecular weight of 63 kDa (released somatotropin is 22 kDa). *In vitro* assay confirms the minimum potency of released somatotropin is NLT 2.5 IU/mg.

SKYTROFA (lonapegsomatropin-tcgd) for injection is a sterile, preservative-free, white to off-white lyophilized powder available in a single-dose, dual-chamber, prefilled cartridge containing lonapegsomatropin-tcgd in one chamber and the diluent, Water for Injection, in the other chamber. SKYTROFA prefilled cartridge must be used with SKYTROFA Auto-Injector to provide an automatic mixing step for reconstitution prior to subcutaneous use.

After reconstitution, each prefilled cartridge delivers:

- 0.273 mL containing 3 mg lonapegsomatropin-tcgd, succinic acid (0.32 mg), trehalose dihydrate (22.7 mg), and tromethamine for pH adjustment to 5.
- 0.327 mL containing 3.6 mg lonapegsomatropin-tcgd, succinic acid (0.39 mg), trehalose dihydrate (27.1 mg), and tromethamine for pH adjustment to 5.
- 0.391 mL containing 4.3 mg lonapegsomatropin-tcgd, succinic acid (0.46 mg) and trehalose dihydrate (32.5 mg) and tromethamine for pH adjustment to 5.
- 0.473 mL containing 5.2 mg lonapegsomatropin-tcgd, succinic acid (0.56 mg) and trehalose dihydrate (39.3 mg) and tromethamine for pH adjustment to 5.
- 0.286 mL containing 6.3 mg lonapegsomatropin-tcgd, succinic acid (0.34 mg) and trehalose dihydrate (21.2 mg) and tromethamine for pH adjustment to 5.
- 0.345 mL containing 7.6 mg lonapegsomatropin-tcgd, succinic acid (0.41 mg) and trehalose dihydrate (25.5 mg) and tromethamine for pH adjustment to 5.
- 0.414 mL containing 9.1 mg lonapegsomatropin-tcgd, succinic acid (0.49 mg) and trehalose dihydrate (30.6 mg) and tromethamine for pH adjustment to 5.
- 0.5 mL containing 11 mg lonapegsomatropin-tcgd, succinic acid (0.59 mg) and trehalose dihydrate (37 mg) and tromethamine for pH adjustment to 5.
- 0.605 mL containing 13.3 mg lonapegsomatropin-tcgd, succinic acid (0.71 mg) and trehalose dihydrate (44.8 mg) and tromethamine for pH adjustment to 5.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

SKYTROFA is a pegylated human growth hormone (somatotropin) for once-weekly subcutaneous injection [*see Pharmacokinetics (12.3)*].

Somatropin binds to the growth hormone (GH) receptor in the cell membrane of target cells resulting in intracellular signal transduction and a host of pharmacodynamic effects. Somatotropin has direct tissue and metabolic effects, and indirect effects mediated by insulin-like growth factor-1 (IGF-1), including stimulation of chondrocyte differentiation and proliferation, stimulation of hepatic glucose output, protein synthesis and lipolysis. Somatotropin stimulates

skeletal growth in pediatric patients with growth hormone deficiency (GHD) as a result of effects on the growth plates (epiphyses) of long bones.

## 12.2 Pharmacodynamics

Somatropin released from SKYTROFA produces a dose linear IGF-1 response, with a change of 0.02 mg/kg on average resulting in a change in IGF-1 standard deviation score (SDS) of 0.17.

At steady-state, IGF-1 levels peak approximately 2 days post-dose, with the average weekly IGF-1 occurring approximately 4.5 days post-dose. IGF-1 levels are in the normal range for GHD patients for the majority of the week, similar to daily somatropin.

## 12.3 Pharmacokinetics

### Absorption

Following subcutaneous dose administration, SKYTROFA releases fully active somatropin via autocleavage of the TransCon linker that follows first-order kinetics.

In pediatric patients with GHD, following subcutaneous dose administration of 0.24 mg/kg/week SKYTROFA, the observed mean (CV%) steady state peak serum concentration ( $C_{max}$ ) of lonapegsomatropin-tcgd was 1230 (86.3) ng hGH/mL, and the median time to reach maximum concentrations ( $T_{max}$ ) was 25 hours. For released somatropin,  $C_{max}$  was 15.2 (83.4) ng/mL with a median  $T_{max}$  of 12 hours. The mean (CV%) somatropin exposure over the one-week dose interval (area under the curve) was 500 (83.8) h\*ng/mL. No significant accumulation of lonapegsomatropin-tcgd and somatropin following repeat dose administration was observed.

$C_{max}$  of the methoxypolyethylene glycol carrier was 13.1 (28.1)  $\mu$ g /mL with a median  $T_{max}$  of 36 hours.

In healthy adults, following single subcutaneous dose administration in the range of 0.24 to 0.42 mg/kg of SKYTROFA, exposure of released somatropin increased greater than proportional to dose.

### Distribution

In pediatric patients with GHD, the mean (CV%) steady state apparent volume of distribution of lonapegsomatropin-tcgd after subcutaneous administration of 0.24 mg/kg/week SKYTROFA was 0.13 (109) L/kg. A similar distribution pattern as observed for daily somatropin is expected once somatropin is released from lonapegsomatropin-tcgd.

### Elimination

#### *Metabolism*

The metabolism of somatropin involves protein catabolism in both the liver and kidneys. The methoxypolyethylene glycol carrier is cleared by the kidneys.

#### *Excretion*

In pediatric patients with GHD, the mean (CV%) lonapegsomatropin-tcgd apparent clearance at steady state was 3.2 (67) mL/h/kg following subcutaneous administration of 0.24 mg/kg/week SKYTROFA with a mean ( $\pm$ SD) observed half-life of 30.7 ( $\pm$ 12.7) hours. The apparent half-life of somatropin released from lonapegsomatropin-tcgd was approximately 25 hours.

### Specific Populations

Based on a population pharmacokinetic analysis, age, sex, race, and body weight do not have clinically meaningful effects on pharmacokinetics.

Male and Female Patients — No sex-specific pharmacokinetic studies have been performed with SKYTROFA. The available literature indicates that the pharmacokinetics of somatropin are similar in men and women.

Patients with Renal or Hepatic Impairment — No specific studies have been performed with SKYTROFA.

## **13 NONCLINICAL TOXICOLOGY**

### **13.1 Carcinogenicity, Mutagenesis, Impairment of Fertility**

Carcinogenicity studies have not been conducted with lonapegsomatropin-tcgd.

Lonapegsomatropin-tcgd was not mutagenic in the Ames test, in the human chromosomal aberration assay or in the rat bone marrow micronucleus test.

In an animal fertility study, lonapegsomatropin-tcgd was administered via subcutaneous injection to male and female rats before cohabitation, through mating to implantation.

Lonapegsomatropin-tcgd did not affect fertility or early embryo-fetal development at doses up to 20-fold the clinical dose of 0.24 mg/kg/week.

## **14 CLINICAL STUDIES**

### **14.1 Treatment-Naïve Pediatric Patients with Growth Hormone Deficiency (NCT02781727)**

A multi-center randomized, open-label, active-controlled, parallel-group phase 3 study was conducted in 161 treatment-naïve, prepubertal pediatric subjects with growth hormone deficiency (GHD); 105 subjects received once-weekly SKYTROFA, and 56 received daily somatropin. The dose in both arms was 0.24 mg/kg/week. The primary efficacy endpoint was annualized height velocity at Week 52.

The subjects ranged in age from 3.2 to 13.1 years with a mean of 8.5 years. One hundred thirty-two (82%) subjects were male and 29 (18%) were female. One subject was Asian, three were Black or African American, 152 were Caucasian, and five were categorized as “other.” The subjects had a mean baseline height SDS (standard deviation score) of -2.9.

Treatment with once-weekly SKYTROFA for 52 weeks resulted in an annualized height velocity of 11.2 cm/year. Subjects treated with daily somatropin achieved an annualized height velocity of 10.3 cm/year after 52 weeks of treatment. Refer to [Table 4](#).

**Table 4: Annualized Height Velocity at Week 52 in Pediatric Treatment-Naïve Subjects with Growth Hormone Deficiency**

	Once-Weekly SKYTROFA (N=105)	Daily Somatropin (N=56)	Estimate of Treatment Difference (95% CI) (SKYTROFA minus Daily Somatropin)
Annualized Height Velocity (cm/year)	11.2	10.3	0.9 (0.2-1.5)

<sup>a</sup> The estimates of least square (LS) means and 95% confidence interval (CI) are from an ANCOVA model that included baseline age, peak GH levels (log transformed) at stimulation test, baseline height SDS – average SDS of parental height as covariates, and treatment and sex as factors. Missing data were imputed with multiple imputation method.

Height SDS (change from baseline) was 1.1 in the SKYTROFA arm and 0.96 in the daily somatropin arm at Week 52. Refer to [Table 5](#).

**Table 5: Height SDS over 52 Weeks in Pediatric Treatment-Naïve Subjects with Growth Hormone Deficiency**

	Once-Weekly SKYTROFA (N=105)	Daily Somatropin (N=56)
Height SDS, baseline	-2.9	-3.0
Height SDS, change from baseline <sup>a</sup>	1.1	0.96

Abbreviations: SDS: Standard deviation score.

<sup>a</sup> Height SDS, change from baseline: The estimates of LS means are from an ANCOVA model that included baseline age, peak GH levels (log transformed) at stimulation test and baseline height SDS as covariates, and treatment and sex as factors.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

### 16.1 How Supplied

SKYTROFA (lonapegsomatropin-tcgd) for injection is a sterile, preservative-free, white to off-white lyophilized powder available in a single-dose, dual-chamber, prefilled cartridge containing lonapegsomatropin-tcgd in one chamber and the diluent, Water for Injection, in the second chamber. The dual-chamber glass cartridge is available in 9 strengths (in somatropin equivalents) as described in [Table 6](#).

**Table 6: SKYTROFA Presentations**

SKYTROFA	NDC
3 mg	73362-003-01
3.6 mg	73362-004-01
4.3 mg	73362-005-01
5.2 mg	73362-006-01
6.3 mg	73362-007-01
7.6 mg	73362-008-01

SKYTROFA	NDC
9.1 mg	73362-009-01
11 mg	73362-010-01
13.3 mg	73362-011-01

Each carton contains 4 single-dose prefilled cartridges and 6 sterile, single-use, disposable 0.25 mm x 4 mm (31-gauge x 5/32 inch) needles. The cartridges are for use only with the SKYTROFA Auto-Injector, packaged in a separate carton. The SKYTROFA Auto-Injector is not supplied with SKYTROFA cartridges but is available for patients with a prescription for SKYTROFA through the Ascendis Pharma Customer Support by calling the toll-free number at 1-844-442-7236 (1-844-44ASCENDIS).

## 16.2 Storage and Handling

- For patients: Refrigerate SKYTROFA cartridges at 36°F to 46°F (2°C to 8°C) in the outer carton to protect from light until the expiration date. Do not freeze. Alternatively, SKYTROFA outer carton containing blistered cartridges may be stored at room temperature [up to 86°F (30°C)] for up to 6 months and can be returned to refrigeration within the 6 months. Write the date first removed from the refrigerator in the space provided on the outer carton. Do not use SKYTROFA beyond the expiration date or 6 months after the date it was first removed from refrigeration (whichever is earlier).
- For pharmacy long-term storage: Store SKYTROFA cartridges refrigerated at 36°F to 46°F (2°C to 8°C) in the outer carton to protect from light until the expiration date. Do not freeze.

## 17 PATIENT COUNSELING INFORMATION

- Provide appropriate instructions for injection to the patient/caregiver, by providing the SKYTROFA Auto-Injector Instructions for Use (available at [www.Skytrofa.com/IFU](http://www.Skytrofa.com/IFU)). Patients/caregivers and healthcare providers may also call the Ascendis Pharma Customer Support toll-free number at 1-844-442-7236 (1-844-44ASCENDIS) for assistance or additional training, if needed.
- Advise patients/caregivers to refer to the Instructions for Use that accompanies the SKYTROFA Auto-Injector for complete mixing and administration instructions with illustrations [see *Preparation and Administration (2.5)*]. Instruct patients/caregivers of proper needle disposal and caution against any reuse of needles. An appropriate container for the disposal of used cartridge and needle should be used.
- Advise patients/caregivers to administer SKYTROFA once weekly, at any time of day. Advise patients/caregivers that doses can be taken 2 days before or 2 days after the scheduled dosing day. Advise patients/caregivers to resume once-weekly dosing for the next dose. If more than 2 days have passed from the scheduled dosing day, advise patients/caregivers to skip the missed dose and take the next dose on the regularly scheduled day. If subsequently changing the regular dosing day to a different day of the week, advise patients/caregivers to ensure that at least 5 days will elapse between the last dose and the newly-established regular dosing day.

- Neoplasms – Advise childhood cancer survivors/caregivers that individuals treated with brain/head radiation are at increased risk of secondary neoplasms and, as a precaution, need to be monitored for recurrence. Advise patients/caregivers to report marked changes in behavior, onset of headaches, vision disturbances and/or changes in skin pigmentation or changes in the appearance of preexisting nevi.
- Glucose Intolerance/Diabetes Mellitus – Advise patients/caregivers that new onset impaired glucose intolerance/type 2 diabetes mellitus or exacerbation of preexisting diabetes mellitus can occur and monitoring of blood glucose during treatment with SKYTROFA may be needed.
- Intracranial Hypertension – Advise patients/caregivers to report to their healthcare provider any visual changes, headache, and nausea and/or vomiting.
- Fluid Retention – Advise patients/caregivers that fluid retention during SKYTROFA replacement therapy may occur. Inform patients/caregivers of the clinical manifestations of fluid retention (e.g., edema, arthralgia, myalgia, nerve compression syndromes including carpal tunnel syndrome/paresthesia) and to report to their healthcare provider if any of these signs or symptoms occur during treatment with SKYTROFA.
- Hypoadrenalism – Advise patients/caregivers that patients who have or who are at risk for pituitary hormone deficiency(s) that hypoadrenalism may develop and to report to their healthcare provider if they experience hyperpigmentation, extreme fatigue, dizziness, weakness, or weight loss.
- Hypothyroidism – Advise patients/caregivers that undiagnosed/untreated hypothyroidism may prevent an optimal response to SKYTROFA. Advise patients/caregivers that patients may require periodic thyroid function tests.
- Pancreatitis – Advise patients/caregivers that pancreatitis may develop and to report to their healthcare provider any new onset abdominal pain.
- Hypersensitivity Reactions – Advise patients/caregivers that serious systemic hypersensitivity reactions (anaphylaxis and angioedema) are possible, and to seek prompt medical attention should an allergic reaction occur.
- Administration: Counsel patients/caregivers that they should never share the SKYTROFA Auto-Injector with another person, even if the needle is changed. Sharing of the Auto-Injector between patients may pose a risk of transmission of infection.

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**PATENT INFORMATION:** [www.ascendispharma.us/products/patents](http://www.ascendispharma.us/products/patents)

Manufactured by:  
Ascendis Pharma Endocrinology Division A/S  
Tuborg Boulevard 12 Hellerup Denmark DK-2900

U.S. License Number XXXX

For information about SKYTROFA contact:

Ascendis Pharma, Inc.

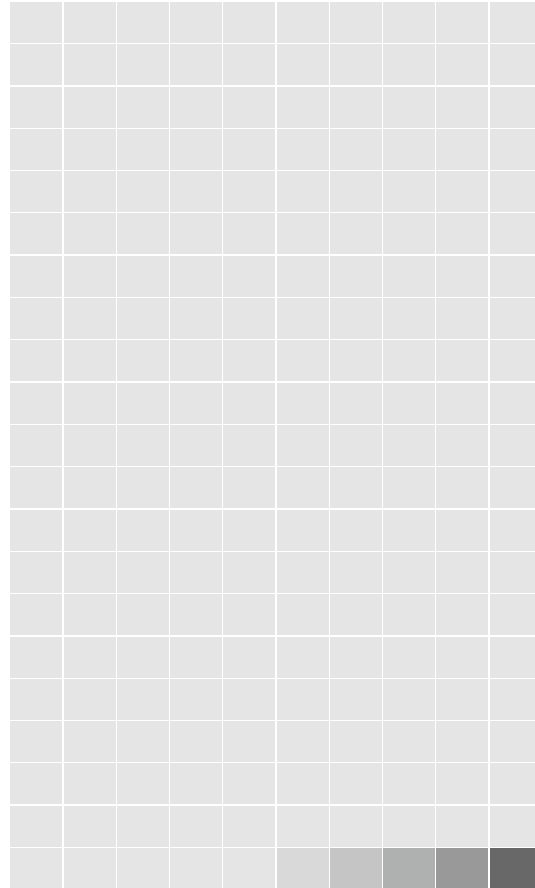
500 Emerson Street

Palo Alto, CA 94301, USA

1-844-442-7236 (1-844-44ASCENDIS)

[www.Skytrofa.com](http://www.Skytrofa.com)

## Keep Track of Your Injections



Device expiration

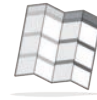
2021-07-16 13500500

## This is your Instructions for Use

- For quick overview of steps, read your Quick Reference Guide
- For training video, go to [www.skytrofa.com](http://www.skytrofa.com)



Instructions  
for Use



Quick  
Reference Guide



[www.skytrofa.com](http://www.skytrofa.com)

Training  
Video

Ascendis Pharma Customer Support



1-844-44ASCENDIS  
(1-844-442-7236)

ascendis  
pharma



### Distributed by:

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This Instructions for Use has been approved by  
the U.S. Food and Drug Administration.  
Approved: Month, Year

# Instructions for Use

**Skytrofa™ Auto-Injector**

For SKYTROFA cartridges

Single-patient use

Watch Video



[www.skytrofa.com](http://www.skytrofa.com)



## Parts Overview

## Getting Started




## How to Use






## Troubleshooting and Care

## Product Information

### Status Icons

-  **Green Check Mark**  
Injection successfully completed
  -  **Green Eye**  
Mixed medicine is ready for inspection in window
  -  **Green Mixing**  
Medicine mixing is in progress
- Read more about status icons on pages 18-33 (and pages 40-47 for troubleshooting)

-  **Constant Green**
  - ➔ Battery is fully charged
  - ➔ The auto-injector is ready to use
-  **Flashing Green**
  - ➔ At least 1 injection remaining, but charging recommended after use

-  **Flashing Red**
    - ➔ Battery needs charging
- Read more about battery status icons on page 17

**Green Top**  
Starts injection when pressed against skin

**Inspection Window**  
Allows for inspection of mixed medicine

**Status Icons**

**Progress Bar**  
Shows progress of mixing and injection

Read more on pages 20-24 and 30-31 (and pages 42-43 for troubleshooting)

**Green Button**  
To turn on the SKYTROFA Auto-Injector or to reject mixed medicine

**Needle**

**SKYTROFA Cartridge**  
Contains medicine and water for injection

**Battery Icon**



- Important Information
- Before You Begin
- Setting Up

- Step-by-Step Guide

Watch Video



[www.skytrofa.com](http://www.skytrofa.com)


- Troubleshooting
- Cleaning and Maintenance
- Charging and Charger Cable
- Storing

- Product Safety
- Expiration
- EMC Compliance Levels
- Technical Specification
- Symbols
- Warranty and Disclaimer
- Parts Overview

## Step-by-step Instructions for the SKYTROFA Auto-Injector

Read and follow this Instructions for Use that comes with your auto-injector before you start using it. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

The back cover of this Instructions for Use folds out for reference while you read the rest of the instructions.

If you have any questions about the auto-injector, the medicine, or these instructions, please contact your healthcare provider or Ascendis Pharma Customer Support. For contact information  back cover.



# Getting Started

Getting Started

## Page

Important Information .....	4
Before You Begin .....	6
Setting Up .....	8

## Important Information

### Important information about your SKYTROFA Auto-Injector:

The auto-injector is used to give (administer) SKYTROFA under your skin (subcutaneously).

Do not use the SKYTROFA Auto-Injector for the first time until you receive training from a healthcare provider. If you do not follow the instructions for the auto-injector, you may not get the right dose, cause injury, or get an infection.

The auto-injector should only be used with SKYTROFA cartridges and needles that are prescribed by your healthcare provider. Cartridges and needles come together in the same packaging. Follow the instructions that come with SKYTROFA cartridges. If refrigerated, take the cartridge out of the refrigerator and leave at room temperature for **15** minutes before use.



Your weekly dose may require that you use 2 cartridges.

**Do not** use your auto-injector with other medicines or needles.

**Do not** share your auto-injector with other people, even if the needle has been changed. You may give other people a serious infection or get a serious infection from them.

**Do not** reuse needles.

**Do not** drop the cartridges because they may break.

**Keep out of the reach of children.**

This product contains small parts that may present a choking hazard to small children. The cable can present a strangulation hazard. The auto-injector should only be used under the supervision of a caregiver.

**Do not** point the auto-injector at yourself or other people, except when you are ready to inject.

**Do not** use or place the auto-injector closer than 12 inches (30 cm) to microwave ovens or electronic equipment with antennas such as mobile phones and WiFi transceivers.

## Before You Begin

### The SKYTROFA Auto-Injector

The auto-injector is an electronic, reusable device for people needing injections of SKYTROFA. It automates parts of the procedure for injecting SKYTROFA. The auto-injector is designed for personal home use, so that the injections may be given without the assistance of a medical professional.

### The SKYTROFA Cartridge

SKYTROFA comes in a single-use cartridge. The cartridge has 2 chambers, 1 filled with powder and 1 filled with water. The auto-injector automatically mixes the powder and the water during preparation, making it ready for injection.

### The Needle

The single-use needle comes with SKYTROFA cartridges and is used for injecting the medicine.

## Product Overview

Charger

USB to  
Micro-USB Cable

Quick Reference  
Guide

Auto-Injector  
Protective Cover

SKYTROFA Auto-Injector



Figure A

## Setting Up


1. Remove the SKYTROFA Auto-Injector from the package.
  2. Connect the USB (large end of the cable) to the charger (only use the provided charger). Plug the charger into a power outlet. Connect the Micro-USB (small end of the cable) to the back of the auto-injector. For protection, charge the auto-injector with the protective cover on (see Figure B).
- For more information on charging  page 49.



Figure B

3. Fully charge the auto-injector before using it for the first time. This will take **2** hours and **30** minutes. When the battery icon located at the base of the auto-injector (see Figure C) is flashing red or green, it is charging. When it shows constant green, the auto-injector is fully charged and is ready to use after the charging cable is unplugged.

- When fully charged, the battery should last for at least **4** injections.
- When traveling, bring your charger and the right adaptor for different power outlets depending on your destination.
- The auto-injector cannot be used when connected to the charger.

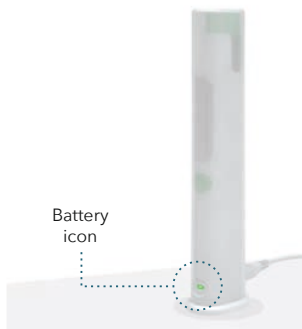


Figure C

## Setting Up

4. Find a quiet place where you can perform your injection.
5. Gather your supplies and place them on a flat, hard, clean surface.

Supplies needed for an injection:

### From SKYTROFA Auto-Injector packaging

(see Figure A):

- 1 SKYTROFA Auto-Injector

### From SKYTROFA packaging

(see Figure D):

- 1 SKYTROFA Cartridge
- 1 Omnican fine 0.25 mm x 4 mm (31G x 5/32") B. Braun needle

### Other supplies (not included)

(see Figure D):

- 1 Alcohol Wipe
- 1 Sharps Container



If your weekly dose requires 2 cartridges, you will need the following additional supplies:

- 1 SKYTROFA Cartridge
- 1 Omnican fine 0.25 mm x 4 mm (31G x 5/32") B. Braun needle
- 1 Alcohol Wipe

## Supplies Needed for Each Injection

Getting Started



Figure D



### **Does Your Weekly Dose Require 2 Cartridges?**

Your healthcare provider may prescribe a dose that requires use of the medicine in 2 cartridges.

If you have been prescribed a dose that requires 2 cartridges:

- Take your first injection (Step 1 to Step 11, pages 14-35).
- Then take your second injection by repeating Step 1 to Step 11 with a new cartridge and needle.
- After your second injection, continue to Step 12 (page 36).

## How to Use

Step-by-Step Guide	Page
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Mix .....	20
Inject .....	26
After Injection .....	32

How to Use

Watch Video



[www.skytrofa.com](http://www.skytrofa.com)

## Prepare

1

### Check and assemble cartridge and needle

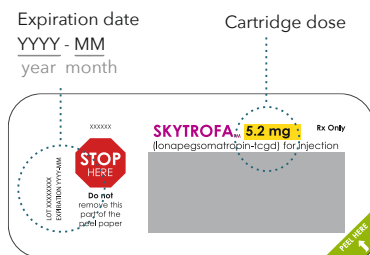



Figure E

#### 1.1 Check the expiration date and cartridge dose on the cartridge packaging (see Figure E).

Remove the SKYTROFA cartridge from the packaging according to the instructions on its lid.

**Do not** use if the expiration date has passed on the cartridge.

- If you are unsure about your dose, contact your healthcare provider.
- If you are unsure about the medicine expiration date, please call Ascendis Pharma Customer Support. For contact information  back cover.

- 1.2 Check the expiration date on the needle. Remove the paper from the needle (see Figure F).

**Do not** use if the expiration date has passed on the needle.

Expiration date  
YYYY - MM - DD  
year month day



Figure F

- 1.3 Screw the needle straight on the cartridge by turning clockwise until there is a **tight fit** (see Figure G).

**Do not** remove the plastic needle cover. You will need it to insert the cartridge into the SKYTROFA Auto-Injector.



Figure G

How to Use



## Prepare

2

### Turn on the auto-injector

Press and release the green button to turn on the auto-injector.




(You will hear **2** loud beeps. Battery icon  will light up and green top will start flashing)

Figure H


**2.1** Disconnect the auto-injector from the charger when charged.

- The auto-injector cannot be used when connected to the charger.


**2.2** Find a quiet place where you can give your injection.

**2.3** Remove the protective cover. Place the auto-injector upright on a flat surface.

**2.4** Press and release the green button to turn on the auto-injector (see Figure H).

- You will hear a humming sound. The battery icon  and the **3** icons above the green button will light up. Then all of the icons will turn off, except the battery icon.

- You will hear **2** loud beeps and the green top will start flashing. The auto-injector is ready for use.
- If the auto-injector is not active for **6** minutes, it will turn off. Press the green button to turn it on again.

**2.5** Check the battery icon on the base of the auto-injector to see if it is charged. The battery icon  is green when the auto-injector is ready to use:



**Constant Green**

Battery is fully charged.  
The auto-injector is ready to use.




**Flashing Green**


At least 1 injection remaining, but charging is recommended after use.



**Flashing Red**

Battery needs charging.

If no icons light up  page 44.

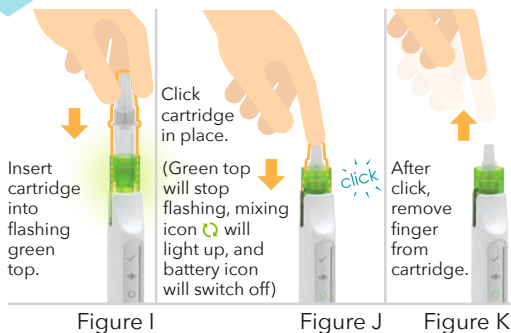
If you see flashing icons (other than the battery)  
 pages 46-47.

How to Use





## Prepare

### 3 Insert cartridge



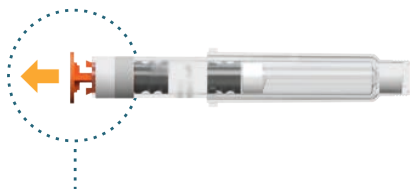
**3.1** Insert the cartridge into the flashing green top by pushing straight down with the needle cover still on (see Figure I).

**3.2** Click the cartridge into place. Make sure the cartridge is pushed all the way down (see Figure J).

- You will hear a click, the green top will stop flashing, the green mixing icon  will light up, and the battery icon  will switch off.
- The cartridge cannot be inserted when the auto-injector is connected to the charger.

**3.3** After the click, remove your finger from the cartridge (see Figure K).


If you cannot insert the cartridge, check if an orange plug is still attached to the cartridge. If an orange plug is still attached to the cartridge, remove it by pulling it straight off (see Figure L). The orange plug only protects the cartridge during transportation.



An orange plug may need to be removed from the cartridge.

Figure L

**Do not** use the auto-injector if you cannot insert the cartridge. Please call Ascendis Pharma Customer Support. For contact information ► back cover.

 If you see a flashing red mixing icon ► page 46.

How to Use



## Mix

4

### Wait while mixing

Wait 4 to 8 minutes for the auto-injector to mix the medicine.

Watch progress bar gradually light up.

Wait 4 to 8 minutes



Wait until you hear **2** loud beeps and the entire progress bar flashes.



Figure M

**4.1** Wait 4 to 8 minutes for the auto-injector to mix your medicine. The progress bar will gradually light up, and you will hear steady ticking during mixing (see Figure M).

- Make sure the auto-injector is standing upright on a flat surface. If the auto-injector is not upright, the medicine mixing will pause.



**4.2** The auto-injector has finished the automatic part of the mixing when you hear **2** loud beeps and the entire progress bar flashes.



**4.3** Continue with Step 5 (page 22) immediately after automatic mixing is completed.

If you wait for more than **2** hours before completing the steps for mixing by hand (Step 5), the auto-injector will automatically cancel the procedure. If this happens, the cartridge will be released and cannot be used. To remove the cartridge, see Step 10 (page 32).

- If you still need to inject after the auto-injector has canceled the procedure, go back to Step 1 and use a new cartridge (page 14).

How to Use

 If you see a slowly flashing green mixing icon and the progress bar is frozen  page 42.

 If you see a flashing red mixing icon  page 46.



## Mix

5

### Turn the auto-injector up and down

Turn the auto-injector up and down. A tick sound confirms the turns are correct.

Turn 5 to 10 times until you hear **2** loud beeps and the progress bar, except the top element, lights up.

**Do not** press the green button.

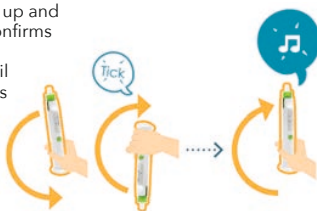


Figure N

**5.1** Turn the auto-injector up and down to mix the medicine by hand. You will hear a 'tick' sound each time you turn the auto-injector up and down correctly. To mix the medicine correctly:

- Each turn up and down should take no more than **2** seconds.
- The auto-injector should point straight down and straight up (see Figure N).

The progress bar, except the top element, will light up as you turn the auto-injector up and down correctly.

**Do not** press the green button when you turn the auto-injector up and down.



After 5 to 10 correct turns, you will hear **2** loud beeps and the progress bar, except the top element, will light up.

**5.2** Continue with Step 6 (page 24) immediately after you finish mixing by hand.

If you wait more than **2** hours before preparing and doing the injection (Step 6 to Step 9, pages 24-31), the auto-injector will automatically cancel the procedure. If this happens, the cartridge will be released and cannot be used. To remove the cartridge, see Step 10 (page 32).

- If you still need to inject after the auto-injector has canceled the procedure, go back to Step 1 and use a new cartridge (page 14).

How to Use

 If you see a flashing red mixing icon  page 46.



## Mix

6

### Finish mixing

Keep upright until you hear **2** loud beeps and the entire progress bar lights up.



Figure O

- 6.1** Keep the auto-injector upright for automatic air removal (see Figure O). Wait until you hear **2** loud beeps and the entire progress bar lights up.



If you see a slowly flashing green mixing icon and the progress bar is frozen

➤ page 42.



If you see a flashing red mixing icon

➤ page 46.

Pull off the needle cover.

**Do not** twist.


**Keep** needle cover for later.

(Eye icon  will light up)



Figure P

How to Use

- 6.2** Pull off the needle cover (see Figure P). The green eye icon  will light up. Removing the needle cover will allow you to check the mixed medicine in the inspection window (Step 7 on page 26).

**Do not** twist the needle cover off. If you have trouble removing the needle cover, gently pull up the green top.

**Keep** the needle cover for later use. It is needed to safely remove the cartridge after injection.



## Inject

7

### Check mixed medicine

Medicine is ok to use if it is colorless and clear (some air bubbles are ok). Go to Step 8.

**Do not** use the mixed medicine if it has visible particles. Press the green button for **3** seconds and go to Step 10.



Figure Q



**7.1** Check the mixed medicine in the inspection window on the side of the auto-injector (see Figure Q). The medicine should look colorless and clear. Some air bubbles are okay.

**Do not** inject the medicine if there are visible particles (medicine is not dissolved) or the mixed medicine is discolored.

If you see visible particles or the medicine is discolored:

- Cancel the injection procedure by pressing and holding the green button for **3** seconds. This will unlock the cartridge. Go to Step 10 (page 32).
- Get a new cartridge. Follow the instructions beginning at Step 1 (page 14).

How to Use

 If you see a flashing red mixing icon  page 46.



## Inject

8

### Prepare for injection

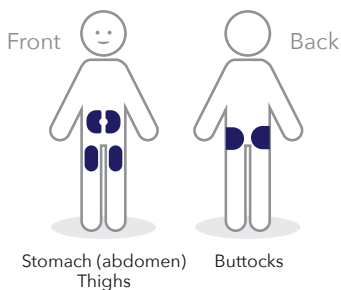


Figure R

**8.1** Choose an injection site.  
There are **3** areas of your body you can inject into (see Figure R):

- Stomach (abdomen)
- Thighs
- Buttocks

Change the injection site for every injection.

- 8.2 Wash your hands with soap and water (see Figure S).



Figure S

- 8.3 Clean the injection site with an alcohol wipe (see Figure T).

**Do not** inject through clothes. Inject directly into the skin.

**Do not** touch the cleaned area before injecting.

**Do not** fan or blow on the cleaned area.

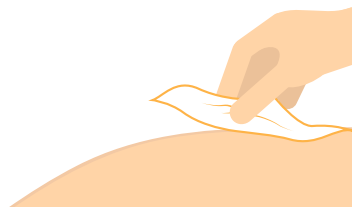


Figure T

How to Use



## Inject

9

### Inject medicine

Press and hold green top against the injection site for **10 to 15** seconds until you hear **2** loud beeps.

(Green top will flash **2** times and check mark icon will light up)



Figure U

Remove the auto-injector from skin and wait until you hear **2** loud beeps.

(Green top will start flashing)




Figure V

**9.1** Press and hold the green top against the skin of the injection site to inject (see Figure U). Hold for **10 to 15** seconds until you hear **2** loud beeps and the green top flashes **2** times. The green check mark icon ✓ will light up.

- The medicine is injected automatically when you press the green top against the skin.
- You will hear steady ticking and the progress bar will light up as you inject.





**Do not** remove the auto-injector from the injection site until the injection is finished to ensure you get your full cartridge dose.

**The injection is finished when you hear 2 loud beeps and the green top flashes 2 times. The green check mark  will light up.**

- 9.2** Remove the auto-injector from the skin after the injection is finished (see Figure V).

- After the injection is finished, the auto-injector makes a buzzing sound as it unlocks the cartridge. Wait until you hear **2** loud beeps, and the green top starts to flash.

How to Use

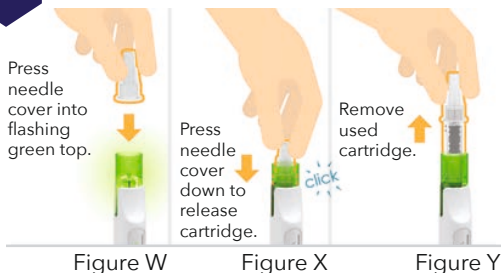
-  If you see a slowly flashing green check mark icon and the progress bar is frozen  page 43.
-  If you see a flashing red check mark icon  page 46.



## After Injection

10

### Remove cartridge



- 10.1** Press the needle cover back on when the green top flashes (see Figure W).


Be careful when handling needles to reduce the risk of needlestick injury and infection.


- 10.2** Press the needle cover down to release the cartridge.

- You will hear a click and the green top will stop flashing (see Figure X).

**Do not** twist the cartridge.

**10.3** Remove the used cartridge by pulling straight up (see Figure Y). Only remove the cartridge by using the needle cover.

- After you remove the cartridge, the battery icon  will display the battery level. The auto-injector turns off automatically.

**Do not** use the auto-injector if you cannot remove the cartridge as instructed. Please call Ascendis Pharma Customer Support. For contact information  back cover.

How to Use



## After Injection

11

### Check cartridge and throw away

Check that cartridge is empty.

Put used cartridge and needle in a sharps disposal container.

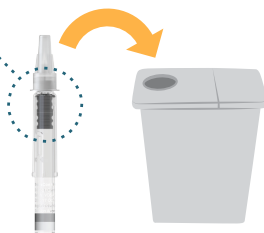



Figure Z

**11.1** Check that the cartridge is empty of medicine (see Figure Z).

**Do not** use the auto-injector if there is medicine left in the cartridge after injection. Please call Ascendis Pharma Customer Support. For contact information  back cover.

**11.2** Put your used cartridge and needle in an FDA-cleared sharps disposal container right away after use (see Figure Z).

**Do not** throw away (dispose of) loose needles and cartridges in your household trash.

**Do not** recycle your used sharps disposal container.

If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:

- Made of a heavy-duty plastic
- Can be closed with a tight-fitting, puncture-resistant lid without sharps being able to come out
- Upright and stable during use
- Leak-resistant
- Properly labeled to warn of hazardous waste inside the container

How to Use

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how to throw away used needles and syringes. For more information about safe sharps disposal, go to the FDA's website at: <http://www.fda.gov/safesharpsdisposal>.

Healthcare providers, relatives, and other caregivers should follow this Instructions for Use for removal and throwing away (disposal) of needles to prevent needlestick injury and infection.



## After Injection



### Does Your Weekly Dose Require 2 Cartridges?

Then take the second injection by repeating Step 1 to Step 11 (pages 14–35) with a new cartridge and needle before continuing to Step 12.

**12**

### Store the auto-injector

Put on the protective cover.

Store at room temperature between 59°F to 86°F (15°C to 30°C), to be ready for next use.

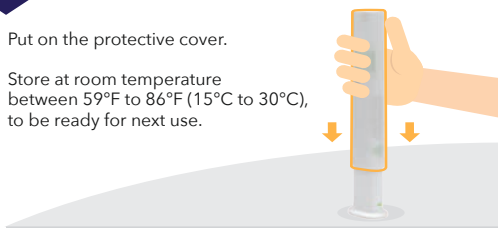




Figure AA


**12.1** Make sure that the auto-injector is clean. If it is dirty or if medicine has been spilled onto it, clean with a damp cloth.


**Do not** place the auto-injector under water. For more information on cleaning ► page 48.

**12.2** Put the protective cover on the auto-injector by sliding it straight down (see Figure AA).

**12.3** Charge the auto-injector if the battery icon has been flashing before or after the injection. For more information about how to charge the auto-injector  page 49.

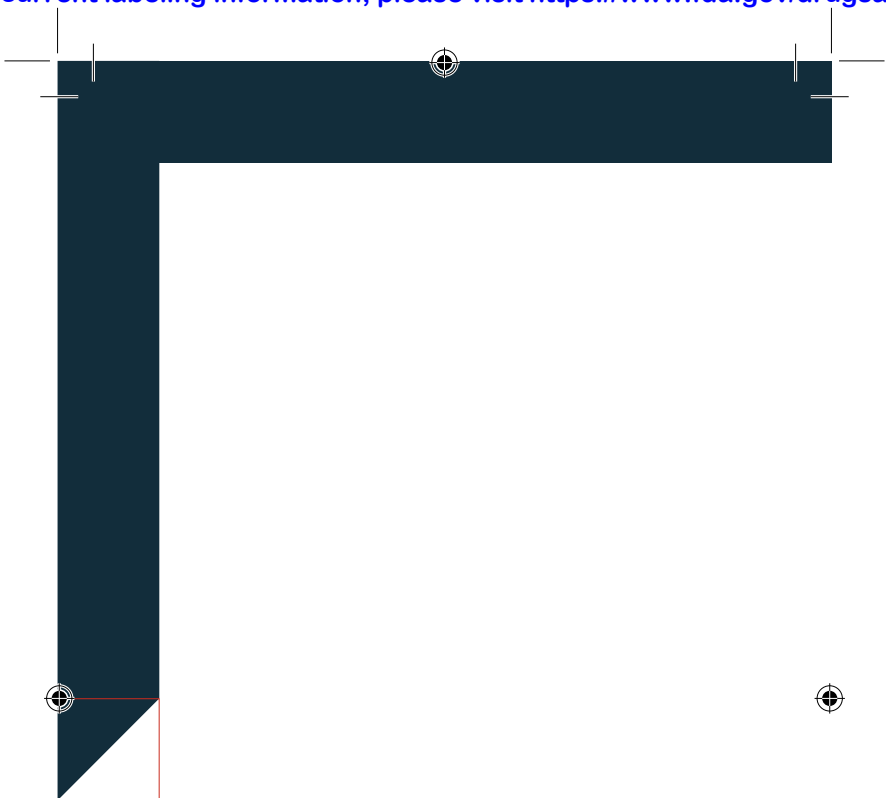
**12.4** Store the auto-injector at room temperature between 59°F to 86°F (15°C to 30°C), between use. Store with the protective cover on until the next injection. For more information about how to store the auto-injector  page 50.

**12.5** Write down the date of every weekly dose taken under Keep Track of Your Injections  back cover fold out.

- When the auto-injector reaches its expiration date, maximum number of injections, or needs replacing, return it to the Ascendis Pharma Customer Support. For more information, see Expiration  page 56.

How to Use





# Troubleshooting and Care

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Troubleshooting  
and Care

## Troubleshooting

- What do you see?

### Green flashing icons

If you see any of these



► pages 42-43.

### Green battery icon

If you see any of these



► page 44.

If you see no icons lighting up at all

► page 44.

40





### Red flashing icons

If you see any  
of these

▀ pages 46–47.




### Red battery icon

If you see this

▀ page 45.

Troubleshooting  
and Care

✓ You see slowly flashing green mixing icon and the progress bar is frozen.

 You hear a repeating warning sound.

**Mixing paused** (Step 4 on page 20). If the SKYTROFA Auto-Injector is not in an upright position, mixing or air removal will pause (see Figure AB).

**Do this:** Place the auto-injector in an upright position and the mixing or air removal will continue.

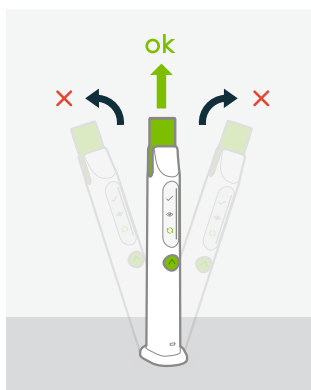


Figure AB



**You see** a slowly flashing **green check mark icon** and the



progress bar is frozen.



**You hear** a repeating warning sound.

**Injection paused** (Step 9 on page 30). If the green top is removed from the skin before completing the injection, the auto-injector will pause the injection (see Figure AC).

**Do this:** Press the green top against skin and the injection will start again. If the injection is not completed within **15** minutes, the auto-injector automatically cancels the injection.

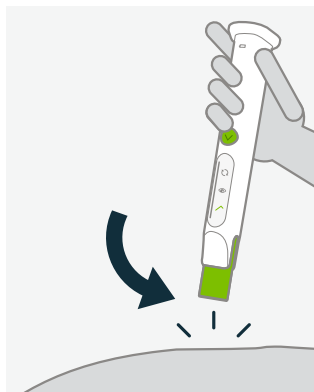


Figure AC



**You see a flashing  
green battery icon.**

**Charging recommended.** There is enough battery for at least **1** injection.

**Do this:** Charge the auto-injector after the next injection.




**You see a constant  
green battery icon.**


**Battery is fully charged.** The auto-injector is ready to use (the battery icon turns off while the auto-injector is in use).

**Do this:** If you are charging the auto-injector, disconnect it from the charger.

**You see no icons lighting up at all.**

**Either the auto-injector has turned off** (the auto-injector will turn off if it is not active for **6** minutes without a cartridge loaded or for **3** minutes with a cartridge loaded) **or the battery needs charging.**

**Do this:** Press the green button to turn it on again. If you see a flashing red battery icon, the battery needs charging. Read more  page 45.

 **You see** a flashing **red battery icon**.  
**You hear** a warning sound.

**The battery needs charging.**

**Do this:** Charge the auto-injector.

Insert the charger cable into the auto-injector at rear lower side and connect to a power outlet (see Figure AD). When the auto-injector has charged for **15** minutes and the battery icon flashes green, the auto-injector is ready to use after the charging cable is unplugged.

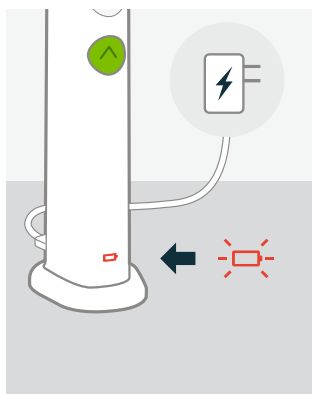




Figure AD

Troubleshooting  
and Care



-  You see a flashing **red mixing icon**.
-  You hear an error sound.



Either you have inserted a used or damaged cartridge, or you have canceled the mixing, or the auto-injector has canceled the injection. The auto-injector cancels the injection **2** hours after automatic mixing (Step 4, page 20) or **2** hours after manual mixing (Step 5, page 22) is completed.

**Do this:** Remove the cartridge and wait for the device to turn off. Start again with a new, unused cartridge and make sure to screw on the needle straight and tightly.

Read more  page 14.

-  You see a flashing **red check mark icon**.
-  You hear an error sound.

Either an injection error has happened (the needle is not screwed on tightly, or it is bent or blocked), or you have canceled the injection, or the auto-injector has canceled an injection that was not completed within 15 minutes.

**Do this:** Remove the cartridge and wait for the auto-injector to turn off. Start again with a new, unused cartridge and make sure to screw on the needle straight and tightly.

Read more  page 14.



**You see** 3 flashing  
green and red icons.

**You hear** a repeating  
error sound.

**The auto-injector is near its expiration.** The first time you see this, either there are 5 injections left or the auto-injector expires in 1 month.

**Do this:** The auto-injector can be used as usual for the remaining injections. When there are no more injections left or the expiration date has passed, the auto-injector cannot be used. Please contact a healthcare provider or Ascendis Pharma Customer Support to receive a new auto-injector. For Ascendis Pharma contact information ► back cover.



**You see** 3 flashing red icons.

**You hear** an error sound.

**Either the auto-injector has expired** (the maximum number of injections has been reached or the lifetime of 5 years has passed) **or a critical error has occurred.**

**Do this:** Try to turn the auto-injector on (press and release the green button). If you still see 3 flashing red icons, the auto-injector needs to be replaced. For disposal information ► page 57. Please contact a healthcare provider or Ascendis Pharma Customer Support to receive a new auto-injector. For Ascendis Pharma contact information ► back cover.

## Cleaning and Maintenance

### Cleaning the SKYTROFA Auto-Injector

If the auto-injector is dirty or if medicine has been spilled onto it, clean with a damp cloth. Before cleaning, the cartridge must be removed.

The green top needs to be cleaned on the outside and on the reachable part of the inside.

If medicine is spilled inside the auto-injector, turn it upside down to let the medicine run out.


**Do not** place the auto-injector in liquid.

**Do not** clean the auto-injector while charging.

**Do not** sterilize the auto-injector.


### Maintenance of the SKYTROFA Auto-Injector


The battery is not replaceable.

**Do not** open, try to repair, or change the auto-injector. Please call Ascendis Pharma Customer Support. For contact information  back cover.

## Charging and Charger Cable

### Charging the SKYTROFA Auto-Injector

Connect the USB (large end of the cable) to the charger. Plug the charger into a power outlet. Connect the Micro-USB (small end of the cable) to the rear of the auto-injector. For protection, charge the auto-injector with the protective cover on. Read more  pages 8-9.

Only charge the auto-injector when the battery icon is flashing green or red. Read more  pages 44-45.

**Do not** attempt to use any charging adaptor or charging cables other than those included with your auto-injector. Other adaptors or cables may create problems and may interfere with device operation.

**Do not** clean the auto-injector while charging.

The auto-injector cannot be used when connected to the charger.

If a cartridge is inserted in the auto-injector, the Micro-USB cannot be connected to the auto-injector. Likewise, a cartridge cannot be inserted into the auto-injector if the Micro-USB is connected to the auto-injector.

## Storing

### Storing the SKYTROFA Auto-Injector

Remove the cartridge from the auto-injector before storing.

Store with the protective cover on.

It is recommended to store the auto-injector at room temperature between 59°F to 86°F (15°C to 30°C), between use. If the auto-injector is stored at higher or lower temperatures, you should keep it at room temperature for 30 minutes before use with a cartridge. The auto-injector can be stored between 14°F to 104°F (-10°C to 40°C) if not in use.

Keep the protective cover on when traveling with the auto-injector.

**Do not** store the auto-injector closer than 12 inches (30 cm) to microwave ovens or electronic equipment with antennas such as mobile phones and WiFi transceivers.

Keep the auto-injector away from dirt, dust, and humid or wet places.

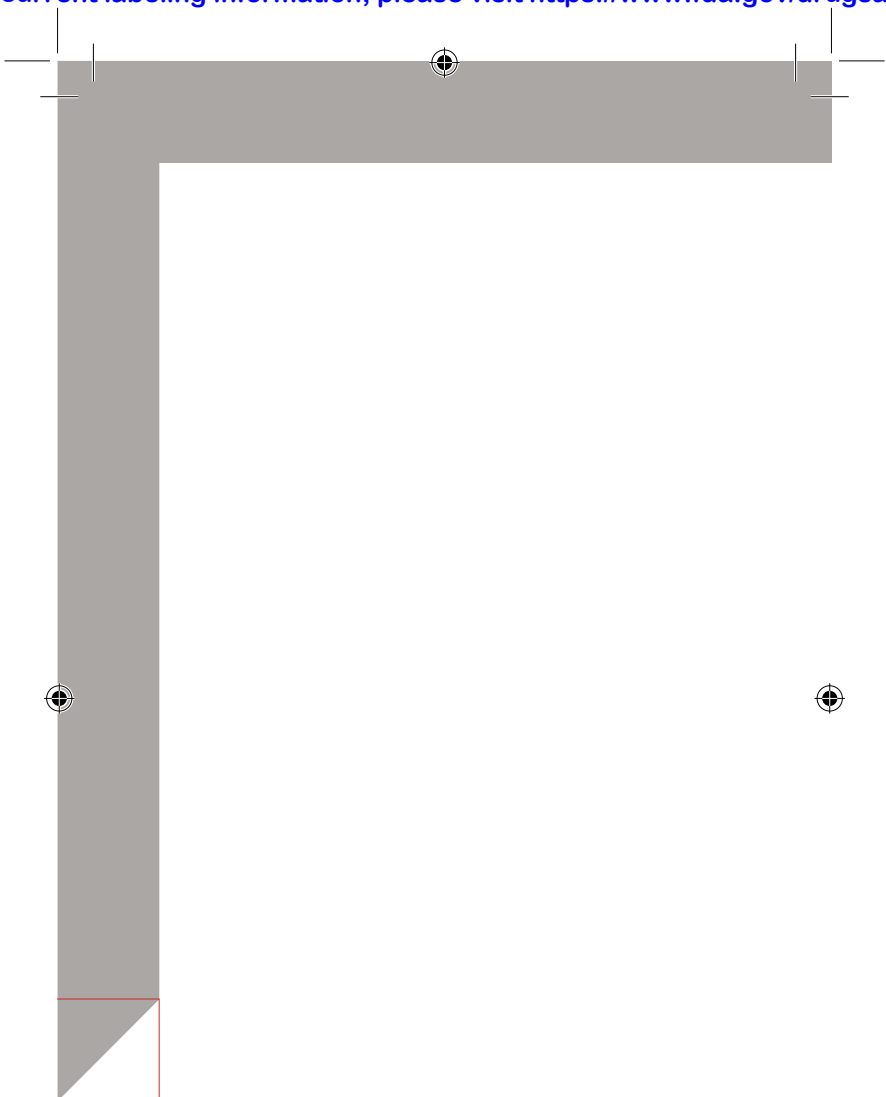
Keep the auto-injector, the charger, and the charging cable away from pets and pests.

Avoid refrigerating or freezing the auto-injector between use.

Avoid exposing the auto-injector to direct sunlight and extreme temperatures.

For technical details of the conditions under which the auto-injector can be used, stored, and transported ► pages 60-61.

Troubleshooting  
and Care



52

# Product Information

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Product  
Information

## Product Safety

**Do not** use the SKYTROFA Auto-Injector if the SKYTROFA cartridge cannot be inserted or removed, or if the cartridge was not completely emptied during the last attempted injection.

**Do not** use the auto-injector if you think it may be damaged.

**Do not** open or change the auto-injector. The auto-injector comes with a battery that cannot be replaced.

**Do not** drop or step on the auto-injector. Extreme vibrations, pressure, or shock, such as a fall onto a hard surface, may damage the auto-injector.

**Do not** drop the cartridges because they may break.

**Do not** clean the auto-injector while charging. Keep the auto-injector dry.

**Do not** place the auto-injector in liquid.

**Do not** wash the auto-injector in a dishwasher.

**Do not** expose the auto-injector to extreme temperatures. Keep the auto-injector away from heat and open flames. Keep it out of direct sunlight.

Keep the auto-injector away from microwave ovens.


**Do not** use or place the auto-injector next to portable RF equipment with antennas such as mobile phones and WiFi transceivers. The auto-injector may not work the right way. Keep RF equipment at least **12 inches (30 cm)** away from the auto-injector when it is being used.


Keep the auto-injector away from areas with high oxygen levels, such as areas where supplemental oxygen is in use.

Product  
Information

## Expiration

The SKYTROFA Auto-Injector has an expiration date (5 years after the manufacturing date) or a maximum of 210 injections, whichever comes first. The expiration date is located at the bottom of the auto-injector and is indicated by year (YYYY), month (MM), and date (DD), printed as YYYY-MM-DD.


When there are 5 injections or less than 1 month left, the auto-injector will indicate this when turned on. Read more  page 47.

The auto-injector may be used for the remaining 5 injections. After the final injection or after the expiration date, your auto-injector has to be replaced. Please contact a healthcare provider or Ascendis Pharma Customer Support to receive a new auto-injector. For contact information  back cover.



The auto-injector contains electrical and electronic components, including a non-replaceable battery.

**Do not** throw away (dispose) in household trash.

When the auto-injector reaches its expiration date, maximum number of injections, or needs replacing, return it to the Ascendis Pharma Customer Support. Contact Ascendis Pharma Customer Support for instructions on how to return properly. For contact information  back cover.

## EMC Compliance Levels

Electromagnetic Compatibility (EMC) Compliance Levels	Basic EMC Standard
EMC - RF Field radiated emission in 10 m (maximum): a) 30 MHz to 230 MHz: ≤ 30 dB (μV/m) quasi-peak. b) 230 MHz to 1 GHz: ≤ 37 dB (μV/m) quasi-peak. c) Internal source <108 MHz	IEC / EN 60601-1-2, 4-th Edition CISPR 11 / EN 55011
EMC - RF Field radiated immunity - Electrical field: a) 10 V/m 80-2700 MHz. 1 kHz 80% AM	IEC / EN 60601-1-2, 4-th Edition IEC 61000-4-3
EMC - Power Frequency Magnetic field, Immunity: a) 30 A/m	IEC / EN 60601-1-2, 4-th Edition IEC 61000-4-3
EMC - Fast transients and bursts: a) Fast transients and bursts ±2 kV ac mains b) Surge ±1 kV Line-to-Line ac mains c) Conducted immunity disturbance by RF fields 3 Vrms 150 kHz to 80 MHz (6 Vrms in ISM and amateur radio bands) d) Conducted emission 150 kHz-30 MHz 120 V @ 60 Hz	IEC / EN 60601-1-2, 4-th Edition IEC 61000-4-4 IEC 61000-4-5 IEC 61000-4-6 IEC 61000-4-11

EMC - Voltage dips and interruptions: a) <5% UT for 5 sec b) <5% UT for 0.5 cycles c) 70% UT for 25 cycles d) 40% UT for 5 cycles	IEC / EN 60601-1-2, 4-th Edition IEC 61000-4-11
EMC - RF Field Immunity to Proximity fields from Wireless communication equipment, Immunity at 0.3 m separation: a) 27 V/m @ 380-390 MHz b) 28 V/m @ 430-470 MHz c) 9 V/m @ 704-787 MHz d) 28 V/m @ 800-960 MHz e) 28 V/m @ 1700-1990 MHz f) 28 V/m @ 2400-2570 MHz g) 9 V/m @ 5100-5800 MHz	IEC / EN 60601-1-2, 4-th Edition IEC 61000-4-39
ESD immunity: a) $\pm$ 8 kV contact b) $\pm$ 2, 4, 8 and 15 kV air	IEC / EN 60601-1-2, 4-th Edition IEC 61000-4-2

Product  
Information

## Technical Specification

SKYTROFA Auto-Injector	
Lifetime	Expiration date ► page 56.
Serial Number (SN)	Please refer to the bottom side of your auto-injector, marked after <b>[SN]</b> .
Size	7.09 x 1.46 x 1.06 in (180 x 37 x 27 mm).
Weight	5.29 oz (150 g).
Display	Light-emitting diodes (LED).
Power source	Mains charger: 100 to 240 V AC.
Power supply	1 rechargeable internal Li-ion battery.
Full capacity charging time	2 hours and 30 minutes. Charging time for 1 injection: 15 minutes.
Full capacity	4 weeks with 1 injection per week.
Electromagnetic compatibility	SKYTROFA Auto-Injector meets the requirements of IEC / EN 60601-1-2, 4-th Edition. Like most electronic devices, using SKYTROFA Auto-Injector in the immediate vicinity of mobile phones or microwave appliances may result in impaired functioning. Use and store SKYTROFA Auto-Injector outside such an environment.
Protection against electric shock	Type BF.
Dose accuracy	According to ISO11608-1:2015.
Ingress protection	IP22: IP2X: Ingress protection of solid foreign objects, $\geq 12.5$ mm diameter. IPX2: Ingress protection of water with harmful effects, dripping (15% tilted). Both put together called IP22.
Cable	USB to Micro-USB cable, 1m.
Charger	
Model	ASSA54a-050100.
Input	100-240V - 50-60Hz.
Output	5.0V $\approx$ 1.0A.

Use Conditions for SKYTROFA Auto-Injector	
Operation temperature (with medicine)	59°F to 86°F (15°C to 30°C) (marking on device bottom).
Storage & Transportation temperature	14°F to 104°F (-10°C to 40°C) (marking on device cover).
Charging temperature	59°F to 86°F (15°C to 30°C).
Operation humidity	15 to 90% relative humidity, non-condensing.
Storage & Transportation relative humidity	Up to 93% relative humidity, non-condensing.
Atmospheric pressure	10.15 psi to 15.37 psi (700 hPa to 1060 hPa).

### Use Conditions for Cartridge with Medicine and Needles

The use conditions provided here are for the SKYTROFA Auto-Injector device. The use conditions for SKYTROFA cartridges with medicine and needles may be different. To see the use conditions for cartridges with medicine and needles, please see the information provided with your medicine.

### Side Effects

For information on side effects, please see the information provided with your medicine.

### Waste









**Regular waste:** Packaging material (not including cartridges) may be thrown away with your household waste.








**Electronic waste:** The auto-injector, including battery, must be returned to the manufacturer. Contact Ascendis Pharma Customer Support for instructions on how to return properly ► back cover.

Charger and USB cable must be disposed of following local regulations for disposal of electronic waste.

## Symbols

These symbols are found on the SKYTROFA Auto-Injector, the packaging, and the Instructions for Use.


	Manufacturer.
	Unique serial number of SKYTROFA Auto-Injector.
	Manufacturer catalogue number for identification.
	Manufacturer batch code for identification.
	Expiration date.
	See Instructions for Use.
	Applied parts SKYTROFA Auto-Injector is a type BF device and provides protection against electrical shock and electrical current leakage. Applied parts on the device are the green top, the housing, and the button.
	Warning! When this symbol is seen, safety instructions must be followed.
Rx only	Caution: Federal law restricts this device for sale by or on the order of a physician.

	<p>Operation temperature.</p>
	<p>Storage &amp; Transportation temperature.</p>
	<p>Keep dry.</p>
	<p>SKYTROFA Auto-Injector complies with the requirements of The Medical Device Directive (MDD 93/42/EEC) and the RoHS (Restriction of Hazardous Substances) directive (2011/65/EU).</p>
	<p>SKYTROFA Auto-Injector contains electrical and electronic components, including a battery that cannot be replaced, and must not be disposed of using standard waste collection.</p>
	<p>SKYTROFA Auto-Injector packaging material is suitable for household waste.</p>
	<p>DC (Direct Current).</p>
 <p>(01) 05713495000077                  (10) 800052690                  (17) 211031                  (21) 18110000123456</p>	<p>The Unique Device Identifier (UDI) that appears on the carton is shown by a barcode and human readable format:                  (01) Device Identifier                  (10) Batch Number                  (17) Expiry date in YYMMDD format                  (21) Serial Number</p>

Product Information

## Warranty and Disclaimer

### Warranty

After the expiration date, your SKYTROFA Auto-Injector must be replaced. Please contact a healthcare provider or Ascendis Pharma Customer Support to receive a new auto-injector. For contact information  back cover.

The expiration date is located at the bottom of the auto-injector and is indicated by year (YYYY), month (MM), and date (DD), printed as YYYY-MM-DD.

### Disclaimer

The correct application of SKYTROFA according to the information provided with your medicine remains your responsibility.

Ascendis Pharma Inc. shall have no liability for incidental or consequential damages.

We reserve the right to modify technical specifications and documentation.

### Patent Information

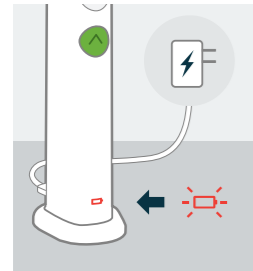
[www.ascendispharma.us/products/patents](http://www.ascendispharma.us/products/patents)

## Quick troubleshooting

For more detailed information, see Instructions for Use (IFU).

### Charging required (Step 2)

IFU page 45



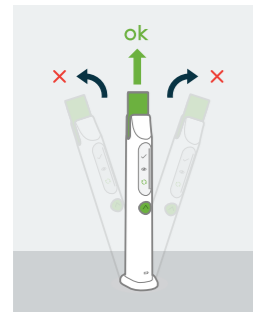
If the battery level is low:

You will see a flashing red battery icon.

**Do this:** Insert charger cable into the SKYTROFA Auto-Injector at rear lower side and connect to a power outlet.

### SKYTROFA Auto-Injector not upright (Step 4 and 6.1)

IFU page 42



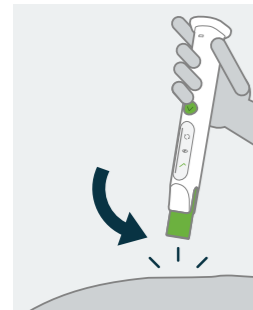
If the SKYTROFA Auto-Injector is not in an upright position during mixing and air removal:

You will hear a repeating warning sound. Mixing icon will flash slowly and progress bar will freeze.

**Do this:** Place the SKYTROFA Auto-Injector in an upright position and the mixing or air removal will continue.

### Skin contact lost (Step 9)

IFU page 43

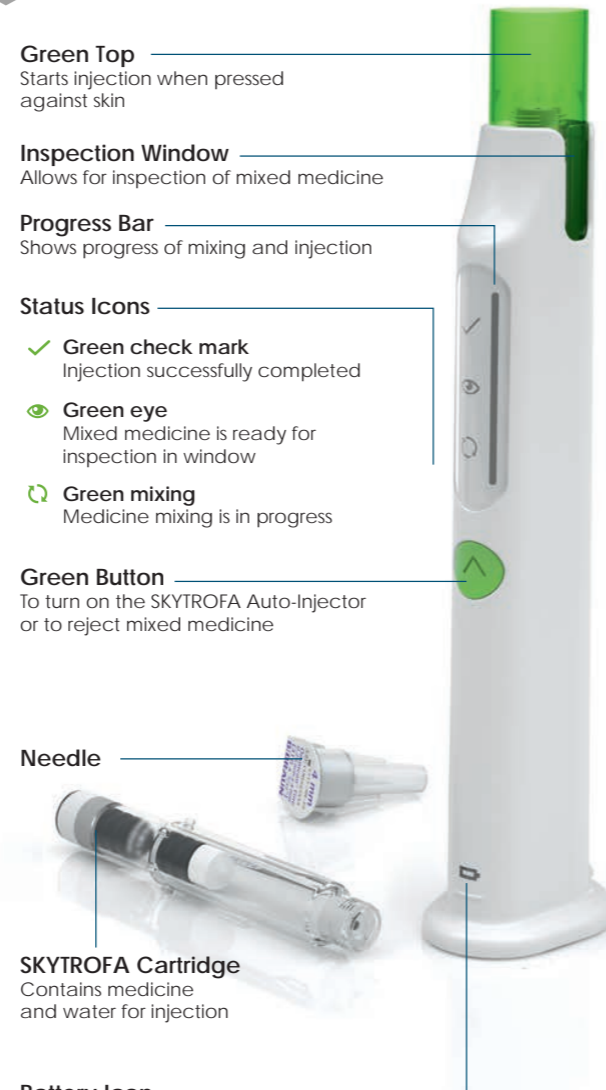


If the green top is removed from skin before the injection is complete:

You will hear a repeating warning sound. Check mark icon will flash slowly and progress bar will freeze.

**Do this:** Press green top against skin and the injection will continue.

## Parts overview



**Green Top**  
Starts injection when pressed against skin

**Inspection Window**  
Allows for inspection of mixed medicine

**Progress Bar**  
Shows progress of mixing and injection

### Status Icons

**Green check mark**  
Injection successfully completed

**Green eye**  
Mixed medicine is ready for inspection in window

**Green mixing**  
Medicine mixing is in progress

**Green Button**  
To turn on the SKYTROFA Auto-Injector or to reject mixed medicine

**Needle**



**SKYTROFA Cartridge**  
Contains medicine and water for injection

### Battery Icon

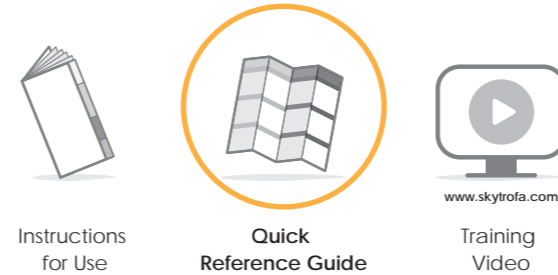
**Constant green**  
➔ Battery is fully charged  
➔ The SKYTROFA Auto-Injector is ready to use

**Flashing green**  
➔ At least 1 injection remaining, but charging recommended after use

**Flashing red**  
➔ Battery needs charging

## This is your Quick Reference Guide

- For full instructions, read your Instructions for Use
- For training video, go to [www.skytrofa.com](http://www.skytrofa.com)
- If you are unsure about your dose, contact your healthcare provider.



Ascendis Pharma Customer Support

1-844-44ASCENDIS  
(1-844-442-7236)

## Quick Reference Guide

**Skytrofa™ Auto-Injector**

For SKYTROFA cartridges

Single-patient use



## Prepare

### 1 Check and assemble cartridge and needle

**1.1** Check expiration date and cartridge dose on cartridge pack.

Expiration date  
YYYY - MM - DD  
year month day

Cartridge dose

**1.2** Check expiration date on needle.

Expiration date  
YYYY - MM - DD  
year month day

**1.3** Screw needle straight and tightly on cartridge. **Do not** remove needle cover.

Remove paper from needle.

### 2 Turn on the auto-injector

Press and release the green button to turn on the auto-injector.

(You will hear 2 loud beeps. Battery icon will light up and green top will start flashing)

### 3 Insert cartridge

**3.1** Insert cartridge into flashing green top.

**3.2** Click cartridge in place. (Green top will stop flashing, mixing icon will light up, and battery icon will switch off)

**3.3** After click, remove finger from cartridge.

Reference ID: 4846899

## Mix

### 4 Wait while mixing

Wait 4 to 8 minutes for the auto-injector to mix medicine.

Wait 4 to 8 minutes

Watch progress bar gradually light up.

Wait until you hear 2 loud beeps and the entire progress bar flashes.

### 5 Turn the auto-injector up and down

Turn the auto-injector up and down. A tick sound confirms the turns are correct. Turn 5 to 10 times until you hear 2 loud beeps and the progress bar, except the top element, lights up.

Do not press the green button.

### 6 Finish mixing

**6.1** Keep upright until you hear 2 loud beeps and the entire progress bar lights up.

**6.2** Pull off needle cover. Do not twist. Keep needle cover for later. (Eye icon will light up)

## Inject

### 7 Check mixed medicine

Medicine is ok to use if it is colorless and clear (some air bubbles are ok). Go to Step 8.

Do not use the mixed medicine if it has visible particles. Press the green button for 3 seconds and go to Step 10.

ok

### 8 Prepare for injection

**8.1** Choose an injection site: Stomach (abdomen), thighs, or buttocks. Change the injection site for every injection.

Front Back

Stomach (abdomen) Thighs Buttocks

**8.2** Wash hands.

**8.3** Clean injection site with alcohol wipe. Do not inject through clothes.

### 9 Inject medicine

**9.1** Press and hold green top against the injection site for 10 to 15 seconds until you hear 2 loud beeps. (Green top will flash 2 times and check mark icon will light up)

**9.2** Remove the auto-injector from skin and wait until you hear 2 loud beeps. (Green top will start flashing)

bzzz

## After injection

### 10 Remove cartridge

**10.1** Press needle cover into flashing green top.

**10.2** Press needle cover down to release cartridge. click

**10.3** Remove used cartridge.

### 11 Check cartridge and throw away

Check that cartridge is empty.

Put used cartridge and needle in a sharps disposal container.

(More info: See Instructions for Use - page 34)

Does your weekly dose require 2 cartridges?

Then take the second injection by repeating Step 1 to Step 11 with a new cartridge and needle before continuing to Step 12.

### 12 Store the auto-injector

Put on the protective cover.

Store at room temperature between 59°F to 86°F (15°C to 30°C), to be ready for next use.