

Published by
Ministry of Health, Labour and Welfare



Translated by
Pharmaceuticals and Medical Devices Agency



This English version is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Revision of Precautions

Somatropin (genetical recombination) (preparations indicated for growth hormone-deficient short stature without epiphyseal closure, short stature without epiphyseal closure associated with Turner's syndrome, short stature without epiphyseal closure associated with chondrodystrophy (achondroplasia, hypochondroplasia), and adult growth hormone deficiency (only in severe cases))

April 4, 2022

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

Therapeutic category

Pituitary hormone preparations

Non-proprietary name

Somatropin (genetical recombination)

Safety measure

Precautions should be revised in the package insert.

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

Revision in line with the Instructions for Package Inserts of Prescription Drugs, PAB Notification No. 606 by the Director General of Pharmaceutical Affairs Bureau, MHW, dated April 25, 1997 (Old instructions): Revised language is underlined.

Current	Revision
<p>Contraindications</p> <p><u>Patients with diabetes mellitus (Growth hormone has anti-insulin-like effects)</u></p> <p>Careful Administration</p> <p>(N/A)</p>	<p>Contraindications</p> <p>(deleted)</p> <p>Careful Administration</p> <p><u>Patients with diabetes mellitus, glucose intolerance, or risk factors of diabetes mellitus (In patients with diabetes mellitus, blood glucose (levels of blood glucose, HbA1c, etc.) and diabetic complications (such as diabetic retinopathy) should be controlled before initiation of administration. After initiation, levels of blood glucose, HbA1c, etc. should be measured periodically and conditions of patients be closely monitored including diabetic complications (such as diabetic retinopathy). Doses of antidiabetic drugs should be adjusted when required. If symptoms of diabetes mellitus become apparent or exacerbated after initiation of administration, appropriate measures should be taken such as dose reduction or temporal discontinuation of this drug. Patients with glucose intolerance or with risk factors of diabetes mellitus (such as obesity and a family history of diabetes mellitus) should be closely monitored. Diabetes mellitus may become apparent.)</u></p>

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

Important Precautions

(N/A)

<Adult growth hormone deficiency>

Levels of blood glucose and HbA1c may rise with administration of this drug. Blood glucose, HbA1c, urinary glucose, etc. should be measured periodically, and dose reduction or discontinuation of administration should be considered if any abnormalities are observed.

Drug Interactions

Precautions for Co-Administration

Drugs	Signs, Symptoms, and Treatment	Mechanism of action
Insulin	<u>Effects of insulin to</u>	Growth hormone <u>has</u>

Important Precautions

<Common to all indications>

Because growth hormone reduces insulin sensitivity, levels of blood glucose and HbA1c may rise with administration of this drug. Levels of blood glucose, HbA1c, etc. should be measured periodically and if any abnormalities are observed, appropriate measures should be taken such as dose reduction or temporal discontinuation of this drug. Particularly in patients with Turner's syndrome, patients may become complicated with reduced glucose tolerance. The clinical course of patients should be monitored closely.

<Adult growth hormone deficiency>

(deleted)

Drug Interactions

Precautions for Co-Administration

Drugs	Signs, Symptoms, and Treatment	Mechanism of action
<u>Antidiabetic drugs</u>	<u>Blood glucose levels</u>	Growth hormone

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

	<u>lower blood glucose may be attenuated.</u>	<u>anti-insulin-like effects.</u>	<u>(insulin preparations, biguanides, sulfonylureas, rapid-acting insulin secretion stimulators, α-glucosidase inhibitors, thiazolidines, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors, etc.)</u>	<u>may rise with administration of this drug. Levels of blood glucose, HbA1c, etc. should be measured periodically and doses of these drugs should be adjusted.</u>	<u>reduces insulin sensitivity.</u>
--	---	-----------------------------------	--	---	-------------------------------------

Adverse Reactions

Other Adverse Reactions

Site	Adverse reactions
Endocrine system ^{Note 2}	Hypothyroidism, reduced glucose tolerance

Note 2: Hypothyroidism may occur or become exacerbated thereby may reduce the treatment effectiveness of this drug. Thyroid function should be tested periodically, and appropriate treatment should preferably be provided in such case. In addition, because glucose tolerance may be reduced, levels of urinary glucose, etc. should preferably be measured periodically. Particularly in patients with

Adverse Reactions

Other Adverse Reactions

Site	Adverse reactions
Endocrine system	Hypothyroidism ^{Note2} , reduced glucose tolerance

Note 2: Hypothyroidism may occur or become exacerbated thereby may reduce the treatment effectiveness of this drug. Thyroid function should be tested periodically, and appropriate treatment should preferably be provided in such case. Particularly in patients with Turner's syndrome, patients may become complicated with thyroid diseases. The clinical course of patients should be closely monitored.

Pharmaceuticals and Medical Devices Agency

Turner's syndrome, patients may become complicated with thyroid diseases <u>or reduced glucose tolerance</u> . The clinical course of patients should be closely monitored.	
---	--

N/A: Not Applicable. No corresponding language is included in the current precautions.

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

Revision in line with the Instructions for Electronic Package Inserts of Prescription Drugs, etc. PSEHB Notification No. 0611-1 by the Director of Pharmaceutical Safety and Environmental Health Bureau, MHLW, dated June 11, 2021 (New instructions): Revised language is underlined.

Current	Revision
<p>2. CONTRAINDICATIONS</p> <p><u>Patients with diabetes mellitus (Growth hormone has anti-insulin-like effects)</u></p> <p>8. IMPORTANT PRECAUTIONS</p> <p><Common to all indications></p> <p>Hypothyroidism may occur or become exacerbated thereby reduce the treatment effectiveness of this drug. Thyroid function should be tested periodically, and appropriate treatment should preferably be provided in such case. <u>In addition, because glucose tolerance may be reduced, urinary glucose, etc. should preferably be measured periodically.</u> Particularly in patients with Turner's syndrome, patients may become complicated with thyroid diseases <u>or reduced glucose tolerance.</u> The clinical course of patients should be monitored closely.</p> <p>(N/A)</p>	<p>2. CONTRAINDICATIONS</p> <p>(deleted)</p> <p>8. IMPORTANT PRECAUTIONS</p> <p><Common to all indications></p> <p>Hypothyroidism may occur or become exacerbated thereby reduce the treatment effectiveness of this drug. Thyroid function should be tested periodically, and appropriate treatment should preferably be provided in such case. Particularly in patients with Turner's syndrome, patients may become complicated with thyroid diseases. The clinical course of patients should be monitored closely.</p> <p><u>Because growth hormone reduces insulin sensitivity, levels of blood glucose and HbA1c may rise with administration of this drug.</u> <u>Levels of blood glucose, HbA1c, etc. should be measured periodically and if any abnormalities are observed, appropriate measures should be taken such as dose reduction or temporal</u></p>

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

<Adult growth hormone deficiency (only in severe cases)>

Levels of blood glucose and HbA1c may rise with administration of this drug. Blood glucose, HbA1c, urinary glucose, etc. should be measured periodically, and dose reduction or discontinuation of administration should be considered if any abnormalities are observed.

9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS

9.1 Patients with Complication or History of Diseases, etc.

(N/A)

discontinuation of this drug. Particularly in patients with Turner's syndrome, patients may become complicated with reduced glucose tolerance. The clinical course of patients should be monitored closely.

<Adult growth hormone deficiency (only in severe cases)>

(deleted)

9. PRECAUTIONS CONCERNING PATIENTS WITH SPECIFIC BACKGROUNDS

9.1 Patients with Complication or History of Diseases, etc.

Patients with diabetes mellitus, glucose intolerance, or risk factors of diabetes mellitus

In patients with diabetes mellitus, blood glucose (levels of blood glucose, HbA1c, etc.) and diabetic complications (such as diabetic retinopathy) should be controlled before initiation of administration.

After initiation, levels of blood glucose, HbA1c, etc. should be measured periodically and conditions of patients be closely monitored including diabetic complications (such as diabetic retinopathy). Doses of antidiabetic drugs should be adjusted when

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp

10. INTERACTIONS

10.2 Precautions for Co-Administration

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
Insulin	<u>Effects of insulin to lower blood glucose may be attenuated.</u>	Growth hormone has <u>anti-insulin-like effects.</u>

required. If symptoms of diabetes mellitus become apparent or exacerbated after initiation of administration, appropriate measures should be taken such as dose reduction or temporal discontinuation of this drug.

Patients with glucose intolerance or with risk factors of diabetes mellitus (such as obesity and a family history of diabetes mellitus) should be closely monitored. Diabetes mellitus may become apparent.

10. INTERACTIONS

10.2 Precautions for Co-Administration

Drugs	Signs, Symptoms, and Treatment	Mechanism and Risk Factors
<u>Antidiabetic drugs (insulin preparations, biguanides, sulfonylureas, rapid-acting insulin secretion stimulators, α-glucosidase inhibitors, thiazolidines, DPP-4 inhibitors, GLP-1 receptor agonists,</u>	<u>Blood glucose levels may rise with administration of this drug. Levels of blood glucose, HbA1c, etc. should be measured periodically and doses of these drugs should be adjusted.</u>	Growth hormone <u>reduces insulin sensitivity.</u>

	<u>SGLT2 inhibitors,</u> <u>etc.)</u>		
--	--	--	--

N/A: Not Applicable. No corresponding language is included in the current precautions.

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp