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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, adult growth hormone deficiency (only in severe cases), and short stature without epiphyseal closure in patients born SGA (small-for-gestational age))

April 4, 2022

Therapeutic category

Pituitary hormone preparations

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Non-proprietary name

Somatropin (genetical recombination)

Safety measure

Precautions should be revised in the package insert.

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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>Precautions Concerning Dosage and Administration</p> <p><u><Short stature associated with Turner's syndrome></u></p> <p><u>When this drug is administered to patients with short stature associated with Turner's syndrome, glucose tolerance should be carefully monitored through periodic testing of oral glucose tolerance, etc.</u></p> <p>Careful Administration</p> <p>(N/A)</p>	<p>Contraindications</p> <p>(deleted)</p> <p>Precautions Concerning Dosage and Administration</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</u></p>

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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

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.)

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 closely monitored..

<Adult growth hormone deficiency>

(deleted)

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observed.

Drug Interactions

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>	<u>Growth hormone has anti-insulin-like effects.</u>

Drug Interactions

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, SGLT2 inhibitors, etc.)</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>	<u>Growth hormone reduces insulin sensitivity.</u>

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

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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>(N/A)</p> <p><u><Short stature without epiphyseal closure associated with Turner's syndrome></u></p> <p><u>Glucose tolerance should be carefully monitored through periodic testing of oral glucose tolerance, etc.</u></p>	<p>2. CONTRAINDICATIONS</p> <p>(deleted)</p> <p>8. IMPORTANT PRECAUTIONS</p> <p><u><Common to all indications></u></p> <p><u>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 when associated with Turner's syndrome, patients may become complicated with reduced glucose tolerance. Conditions of patients should be closely monitored.</u></p> <p>(deleted)</p>

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

Levels of blood glucose and HbA1c may rise with administration of this drug. Blood glucose, HbA1c, or 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)

<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 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

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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>

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, SGLT2 inhibitors, etc.)</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>

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

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