פייזר פרמצבטיקה ישראל בע"מ
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יולי 2022

רופא/ה, רוקח/ת נכבד/ה,
ברצוננו להודיעך על עדכון בעלון לרופא עבור:

GENOTROPIN 5.3MG
GENOTROPIN 12MG

<u>התוויה</u>

Children:
Short stature due to inadequate or failed secretion of pituitary growth hormone or Turner`s syndrome. Short stature in children with renal insufficiency.
Growth disturbance (height SDS<2.5 and parenteral adjusted height SDS < -1) in short children born SGA (SGA - small for gestational age i.e. born small in relation to the length of the fetus development) with a birth weight and/or length < 2 SD who failed to show catch up growth (HV SDS < 0 during the last year) by 4 years of age or later.
Prader willi syndrome for improvement of growth and body composition.
Adults:
For adults who have suffered from growth-hormone deficiency since childhood.
For adults who have aquired growth hormone deficiency due to a pituitary pathology causing hypopituitarism.

<u>להלן העדכונים העיקריים בעלון לרופא:</u>

4.8 Undesirable effects

<u>Tabulated list of adverse reactions</u>
Table~~s~~ 1 ~~-6~~ shows the adverse reactions ranked under headings of System Organ Class and frequency <u>for children and adults</u>, using the following convention: very common (≥1/10); common (≥1/100 to < 1/10); uncommon (≥1/1,000 to < 1/100); rare (≥1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data) ~~for each of the indicated conditions.~~

Table 1: Tabulated list of adverse reactions

System organ class	Very common (≥1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)	Rare (≥1/10,000 to <1/1000)	Very rare (<1/10,000)	Not known (cannot be estimated from available data)
Neoplasms benign, malignant, and unspecified (including cysts and polyps)			(Children) Leukaemia†			
Metabolism and nutrition disorders						(Adults and Children) Type 2 diabetes mellitus

Tabulated list of adverse reactions

Tables ~~1-6~~ shows the adverse reactions ranked under headings of System Organ Class and frequency for children and adults, using the following convention: very common (≥1/10); common (≥1/100 to < 1/10); uncommon (≥1/1,000 to < 1/100); rare (≥1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data) ~~for each of the indicated conditions.~~

Table 1: Tabulated list of adverse reactions

System organ class	Very common (≥1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)	Rare (≥1/10,000 to <1/1000)	Very rare (<1/10,000)	Not known (cannot be estimated from available data)
Nervous system disorders		(Adults) Paraesthesia* (Adults) Carpal tunnel syndrome	(Children) Benign intracranial hypertension (Children) Paraesthesia*			(Adults) Benign intracranial hypertension
Skin and subcutaneous tissue disorders			(Children) Rash**, Pruritus**, Urticaria**			(Adults) Rash**, Pruritis**, Urticaria**
Musculoskeletal and connective tissue disorders	(Adults) Arthralgia*	(Adults) Myalgia* (Adults) Musculoskeletal stiffness* (Children) Arthralgia*	(Children) Myalgia*			(Children) Musculoskeletal stiffness*
Reproductive system and breast disorders			(Adults and Children) Gynaecomastia			
General disorders and administration site conditions	(Adults) Oedema peripheral*	(Children) Injection-site reaction$	(Children) Oedema peripheral*			(Adults and Children) Face oedema* (Adults) Injection-site reaction$
Investigations						(Adults and Children) Blood cortisol decreased‡

* In general, these adverse effects are mild to moderate, arise within the first months of treatment, and subside spontaneously or with dose-reduction. The incidence of these adverse effects is related to the administered dose, the age of the patients, and possibly inversely related to the age of the patients at the onset of growth hormone deficiency.

** Adverse Drug Reactions (ADR) identified post-marketing.

$ Transient injection site reactions in children have been reported.

‡ Clinical significance is unknown

† Reported in growth hormone deficient children treated with somatropin, but the incidence appears to be similar to that in children without growth hormone deficiency.

Clinical Trials in Children with GHD

Table 1

Long-term Treatment of Children with Growth Disturbance due to insufficient secretion of growth hormone

System Organ Class	Very Common ≥1/10	Common ≥1/100 to <1/10	Uncommon ≥1/1,000 to <1/100	Rare ≥1/10,000 to <1/1,000	Very Rare <1/10,000	Not Known (cannot be estimated from available data)
Neoplasms Benign, Malignant and Unspecified (including cysts and polyps)			Leukaemia†			
Metabolism and Nutrition Disorders						Type 2 diabetes mellitus
Nervous System Disorders						Paraesthesia* Benign intracranial hypertension
Skin and Subcutaneous Tissue Disorders			Rash** Pruritus** Urticaria**			
Musculoskeletal, Connective Tissue and Bone Disorders			Arthralgia*			Myalgia* Musculoskeletal stiffness*
Reproductive System and Breast Disorders			Gynaecomastia			
General Disorders and Administration Site Conditions	Injection site reaction$					Oedema peripheral* Face oedema*
Investigations						Blood cortisol decreased‡

*In general, these adverse effects are mild to moderate, arise within the first months of treatment, and subside spontaneously or with dose reduction. The incidence of these adverse effects is related to the administered dose, the age of the patients, and possibly inversely related to the age of the patients at the onset of growth hormone deficiency.

** Adverse Drug Reactions (ADR) identified post-marketing

$ Transient injection site reactions in children have been reported.

‡ Clinical significance is unknown

† Reported in growth hormone deficient children treated with somatropin, but the incidence appears to be similar to that in children without growth hormone deficiency.

Clinical Trials in children with Turner Syndrome

Table 2

Long-term Treatment of Children with Growth Disturbance due to Turner syndrome

System Organ Class	Very Common ≥1/10	Common ≥1/100 to <1/10	Uncommon ≥1/1,000 to <1/100	Rare ≥1/10,000 to <1/1,000	Very Rare <1/10,000	Not Known (cannot be estimated from available data)
Neoplasms Benign, Malignant and Unspecified (including cysts and polyps)						Leukaemia†
Metabolism and Nutrition Disorders						Type 2 diabetes mellitus
Nervous System Disorders						Paraesthesia* Benign intracranial hypertension
Skin and Subcutaneous Tissue Disorders						Rash** Pruritus** Urticaria**
Musculoskeletal, Connective Tissue and Bone Disorders	Arthralgia*					Myalgia* Musculoskeletal stiffness*
Reproductive System and Breast Disorders			Gynaecomastia			
General Disorders and Administration Site Conditions						Oedema peripheral* Face oedema* Injection site reaction$
Investigations						Blood cortisol decreased‡

*In general, these adverse effects are mild to moderate, arise within the first months of treatment, and subside spontaneously or with dose reduction. The incidence of these adverse effects is related to the administered dose, the age of the patients, and possibly inversely related to the age of the patients at the onset of growth hormone deficiency.

** Adverse Drug Reactions (ADR) identified post-marketing.

$ Transient injection site reactions in children have been reported.

‡ Clinical significance is unknown

† Reported in growth hormone deficient children treated with somatropin, but the incidence appears to be similar to that in children without growth hormone deficiency.

Clinical Trials in Children with Chronic Renal Insufficiency

Table 3

Long-Term Treatment of Children with Growth Disturbance due to Chronic Renal Insufficiency

System Organ Class	Very Common ≥1/10	Common ≥1/100 to <1/10	Uncommon ≥1/1000 to <1/100	Rare ≥1/10,000 to <1/1000	Very Rare <1/10,000	Not Known (cannot be estimated from available data)
Neoplasms Benign, Malignant, and Unspecified (including cysts and polyps)						Leukaemia†
Metabolism and Nutrition Disorders						Type 2 diabetes mellitus
Nervous System Disorders						Paraesthesia* Benign intracranial hypertension
Skin and Subcutaneous Tissue Disorders		Rash**				Pruritus** Urticaria**
Musculoskeletal, Connective Tissue, and Bone Disorders						Arthralgia* Myalgia* Musculoskeletal stiffness*
Reproductive System and Breast Disorders			Gynaecomastia			
General Disorders and Administration Site Conditions		Injection site reaction$				Oedema peripheral* Face oedema*
Investigations						Blood cortisol decreased‡

*In general, these adverse effects are mild to moderate, arise within the first months of treatment, and subside spontaneously or with dose reduction. The incidence of these adverse effects is related to the administered dose, the age of the patients, and possibly inversely related to the age of the patients at the onset of growth hormone deficiency.

** Adverse Drug Reactions (ADR) identified post-marketing.

$ Transient injection site reactions in children have been reported.

‡ Clinical significance is unknown.

† Reported in growth hormone deficient children treated with somatropin, but the incidence appears to be similar to that in children without growth hormone deficiency.

Clinical Trials in children with SGA

Table 4

Long-term Treatment of Children with Growth Disturbance due to Born Small for Gestational Age

System Organ Class	Very Common ≥1/10	Common ≥1/100 to <1/10	Uncommon ≥1/1,000 to <1/100	Rare ≥1/10,000 to <1/1,000	Very Rare <1/10,000	Not Known (cannot be estimated from available data)
Neoplasms Benign, Malignant and Unspecified (including cysts and polyps)						Leukaemia†
Metabolism and Nutrition Disorders						Type 2 diabetes mellitus
Nervous System Disorders						Paraesthesia* Benign intracranial hypertension
Skin and Subcutaneous Tissue Disorders		Rash** Urticaria **	Pruritus**			
Reproductive System and Breast Disorders			Gynaecomastia			
Musculoskeletal, Connective Tissue and Bone Disorders			Arthralgia*			Myalgia* Musculoskeletal stiffness*
General Disorders and Administration Site Conditions		Injection site reaction$				Oedema peripheral* Face oedema*
Investigations						Blood cortisol decreased‡

*In general, these adverse effects are mild to moderate, arise within the first months of treatment, and subside spontaneously or with dose reduction. The incidence of these adverse effects is related to the administered dose, the age of the patients, and possibly inversely related to the age of the patients at the onset of growth hormone deficiency.

** Adverse Drug Reactions (ADR) identified post-marketing.

$ Transient injection site reactions in children have been reported.

‡ Clinical significance is unknown

† Reported in growth hormone deficient children treated with somatropin, but the incidence appears to be similar to that in children without growth hormone deficiency.

Clinical Trials in PWS

Table 5

Long-term Treatment and Improvement of Body Composition of Children with Growth Disturbance due to Prader-Willi Syndrome

System Organ Class	Very Common ≥1/10	Common ≥1/100 to <1/10	Uncommon ≥1/1,000 to <1/100	Rare ≥1/10,000 to <1/1,000	Very Rare <1/10,000	Not Known (cannot be estimated from available data)
Neoplasms Benign, Malignant and Unspecified (including cysts and polyps)						Leukaemia†
Metabolism and Nutrition Disorders						Type 2 diabetes mellitus
Nervous System Disorders		Paraesthesia*				
		Benign intracranial hypertension				
Skin and Subcutaneous Tissue Disorders		Rash**				Pruritus**
						Urticaria**
Musculoskeletal, Connective Tissue and Bone Disorders		Arthralgia*				Musculoskeletal stiffness*
		Myalgia*				
Reproductive System and Breast Disorders			Gynaecomastia			
General Disorders and Administration Site Conditions		Oedema peripheral*				Face oedema*
						Injection site reaction$
Investigations						Blood cortisol decreased‡

*In general, these adverse effects are mild to moderate, arise within the first months of treatment, and subside spontaneously or with dose reduction. The incidence of these adverse effects is related to the administered dose, the age of the patients, and possibly inversely related to the age of the patients at the onset of growth hormone deficiency.

** Adverse Drug Reactions (ADR) identified post-marketing.

$ Transient injection site reactions in children have been reported.

‡ Clinical significance is unknown

† Reported in growth hormone deficient children treated with somatropin, but the incidence appears to be similar to that in children without growth hormone deficiency.

Clinical Trials in Adults with GHD

Table 6

Replacement Therapy in Adults with Growth Hormone Deficiency

System Organ Class	Very Common ≥1/10	Common ≥1/100 to <1/10	Uncommon ≥1/1,000 to <1/100	Rare ≥1/10,000 to <1/1,000	Very Rare <1/10,000	Not Known (cannot be estimated from available data)
Metabolism and Nutrition Disorders						Type 2 diabetes mellitus
Nervous System Disorders		Paraesthesia* Carpal Tunnel Syndrome				Benign intracranial hypertension
Skin and Subcutaneous Tissue Disorders						Rash** Pruritus** Urticaria**
Musculoskeletal, Connective Tissue and Bone Disorders	Arthralgia*	Myalgia* Musculoskeletal stiffness*				
Reproductive System and Breast Disorders			Gynaecomastia			
General Disorders and Administration Site Conditions	Oedema peripheral*					Face oedema* Injection site reaction$
Investigations						Blood cortisol decreased‡

*In general, these adverse effects are mild to moderate, arise within the first months of treatment, and subside spontaneously or with dose reduction. The incidence of these adverse effects is related to the administered dose, the age of the patients, and possibly inversely related to the age of the patients at the onset of growth hormone deficiency.

** Adverse Drug Reactions (ADR) identified post-marketing.

$ Transient injection site reactions in children have been reported.

‡ Clinical significance is unknown

Leukaemia

Cases of leukaemia (rare or very rare) have been reported in children with a GH deficiency, some of whom were treated with somatropin and included in the post-marketing experience. However, there is no evidence of an increased risk of leukaemia without predisposition factors, such as radiation to the brain or head.

להלן העדכונים העיקריים בעלון לצרכן:

4. תופעות לוואי

תופעות לוואי שכיחות (עשויות להופיע בעד-1 מ-10 מטופלים):

בילדים:

- כאב מפרקים
- אדמומיות, עקצוץ או כאב חולפים באזור ההזרקה.
- ~~כאב מפרקים~~
- ~~פריחה~~
- ~~בליטות מגרדות על פני העור~~

במבוגרים:

- חוסר תחושה/עקצוץ.
- תחושת כאב או שריפה בידיים או בבית השחי (תסמונת מנהרת שורש כף היד, Carpal Tunnel Syndrome).
- נוקשות בזרועות וברגליים, כאב שרירים.
- ~~תחושת כאב או שריפה בידיים או בבית השחי (תסמונת מנהרת שורש כף היד, Carpal Tunnel Syndrome).~~

תופעות לוואי שאינן שכיחות (עשויות להופיע בעד-1 מ-100 מטופלים):

בילדים:

- לוקמיה (דווח במספר קטן של מטופלים עם מחסור בהורמון גדילה, חלקם טופלו עם סומטרופין. עם זאת, אין הוכחה לכך שיש עלייה בשכיחות הלוקמיה במטופלים ללא גורמי סיכון המקבלים הורמון גדילה).
- לחץ תוך גולגולתי מוגבר (הגורם לתסמינים כגון כאב ראש חזק, הפרעות בראייה או הקאה).
- חוסר תחושה/עקצוץ.
- פריחה
- גרד
- בליטות מגרדות על פני העור
- כאבי שרירים
- חזה מוגדל (גניקומסטיה).
- אצירת מים (אשר מתבטאת באצבעות נפוחות או קרסוליים נפוחים לפרק זמן קצר בתחילת הטיפול).
- ~~גרד~~
- ~~חזה מוגדל (גניקומסטיה).~~

במבוגרים:

- חזה מוגדל (גניקומסטיה).

~~תופעות לוואי נדירות (עשויות להופיע בעד-1 מ-1000 מטופלים):~~

~~בילדים:~~

- ~~חוסר תחושה/עקצוץ.~~
- ~~לוקמיה (דווח במספר נמוך של מטופלים בעלי חוסר בהורמון גדילה, חלקם טופלו עם סומאטרופין. עם זאת אין הוכחה לכך שיש עלייה בשכיחות לוקמיה במטופלים ללא גורמי סיכון המקבלים הורמון גדילה).~~
- ~~לחץ תוך-גולגולתי מוגבר (הגורם לתסמינים כגון כאב ראש חזק, הפרעות בראייה או הקאה).~~
- כאב שרירים.

תופעות לוואי ששכיחותן אינה ידועה, לא ניתן להעריך את השכיחות מהמידע הקיים:

- סוכרת סוג 2.
- נפיחות בפנים.
- ירידה ברמות ההורמון קורטיזול בדם.
- ~~נפיחות בפנים.~~

בילדים:

- נוקשות בזרועות וברגליים.

במבוגרים:

- לחץ תוך-גולגולתי מוגבר (הגורם לתסמינים כגון כאב ראש חזק, הפרעות בראייה או הקאה).
- פריחה.
- גרד.
- בליטות מגרדות על פני העור.
- אדמומיות, עקצוץ או כאב באזור ההזרקה.
- ~~פריחה.~~
- ~~גרד.~~
- ~~בליטות מגרדות על פני העור.~~

השינויים המודגשים ברקע צהוב מהווים החמרה. כמו כן, בוצעו שינויים נוספים הכוללים תוספת מידע, השמטת מידע ועדכוני נוסח שאינם מהווים החמרה .

העלונים המעודכני ם נשל חו למשרד הבריאות לצורך פרסומם במאגר התרופות שבאתר משרד הבריאות:

https://israeldrugs.health.gov.il/#!/byDrug

לחילופין, לקבלת עלון מלא מודפס ניתן לפנות לחברת פייזר פרמצבטיקה ישראל בע"מ, שנקר 9 , ת.ד. 12133 הרצליה פיתוח, 46725 .

בברכה,
אורטל עבודי
רוקחת ממונה