



**FOR IMMEDIATE RELEASE**

**FDA Approves Norditropin<sup>®</sup> for Treatment of Short Stature Associated with a Rare Genetic Disorder**

***Norditropin is the only growth hormone therapy indicated for short stature in children with Noonan syndrome***

**PRINCETON, N.J., June 1, 2007** – Novo Nordisk today announced that Norditropin<sup>®</sup> (somatotropin [rDNA origin] injection) received U.S. Food and Drug Administration (FDA) approval for the treatment of short stature in children with Noonan syndrome. Noonan syndrome is defined as an autosomal dominant genetic syndrome commonly characterized by short stature, congenital heart defects, and unique facial features. The appearance of this disorder can include hypertelorism (widely-set eyes), down-slanting eyes, webbed neck, and other conditions, including congenital heart disease in half of those affected. Up to 80 percent of children with Noonan syndrome suffer from significant short stature.

“When you see a child who has Noonan syndrome, it may not always be obvious to the naked eye, but the complications associated with the condition are quite serious and can affect both physical development and other systems” said Martin Soeters, president of Novo Nordisk Inc. “There are few treatment options available to help the physical development, and this approval marks an exciting advancement for children with this rare condition.”

Noonan syndrome is classified as a rare condition with a population of less than 200,000. To encourage the development of treatments for rare disorders – that may not otherwise be commercially viable for development – the FDA designates drugs that treat fewer than 200,000 patients with an “orphan drug” designation.

Norditropin has received orphan drug designation for the treatment of short stature associated with Noonan syndrome.

**Novo Nordisk Inc.**

An Phan  
100 College Road West  
Princeton, New Jersey 08540  
USA

Telephone: (609)987-5800  
Direct dial: (609)987-4893  
Telefax: (609)919-7801

E-mail: [anph@novonordisk.com](mailto:anph@novonordisk.com)

### ***About Noonan Syndrome***

The prevalence of Noonan syndrome has not been determined accurately to date, but most authors report 1 in 1,000 - 2,500 live births, affecting males and females equally. Based on the United States population, prevalence may range anywhere from 125,000 to 300,000 live births. However, fetal loss can occur in Noonan syndrome so actual incidence of the disorder may be higher than its prevalence.

### **Clinical Features and Complications**

- Unique facial features, such as widely-spaced eyes, triangular face, low-set ears, and short-webbed neck
- Short stature (up to 80% of individuals)
- Congenital heart defects
- Abnormal chest (shrunken sternum or concave chest)
- Undescended testes in males (more than 50%)
- Bleeding disorders, and easy bruising, especially Factor XI (clotting factor) deficiency (which causes Hemophilia C)
- Feeding difficulties with babies, including poor suckling and weaning; frequent or forceful vomiting may also occur
- Common eye problems including near sightedness and a squint
- Hearing problems caused by middle ear infections
- Poor muscle tone in early development
- Lymphatic system problems, such as lymphedema

There is no specific pharmacologic therapy currently available, and treatment for Noonan syndrome focuses on its clinical features and complications.

“Noonan syndrome is a heterogeneous genetic condition in which the clinical features are quite variable. Short stature, which can be severe, is one of the most common characteristics. Treatment with Norditropin may help children with Noonan syndrome improve one of the most concerning physical features of the condition,” said Alicia Romano, M.D., Pediatric Endocrinologist, New York Medical College.

### ***About Norditropin***

Norditropin® (somatropin [rDNA origin] injection) is indicated for the treatment of children with short stature associated with Noonan syndrome, treatment of children with growth failure due to inadequate secretion of endogenous growth hormone and for replacement of endogenous growth hormone in adults with growth hormone deficiency (GHD) who meet either of the following two criteria:

- 1) Adult Onset: Patients who have GHD, either alone or associated with multiple hormone deficiencies (hypopituitarism), as a result of pituitary disease, hypothalamic disease, surgery, radiation therapy, or trauma; or
- 2) Childhood Onset: Patients who were growth hormone deficient during childhood as a result of congenital, genetic, acquired, or idiopathic causes.

In general, confirmation of the diagnosis of adult GHD in both groups usually requires an appropriate growth hormone stimulation test.

### **Important Safety Information**

Somatropin should not be used for growth promotion in pediatric patients with closed epiphyses or in patients with active proliferative or severe non-proliferative diabetic retinopathy. Norditropin should not be used in patients with known hypersensitivity to somatropin or any of its excipients.

Somatropin should not be used or should be discontinued with any evidence of active malignancy. Patients with preexisting malignancy should be monitored carefully for any progression or reoccurrence.

Somatropin should not be used to treat patients with acute critical illness due to complications following open heart or abdominal surgery, multiple accidental trauma or acute respiratory failure as increased mortality may occur.

Deaths have been reported in patients with Prader-Willi syndrome who are severely obese or have severe respiratory impairment and are treated with somatropin. Unless patients with Prader-Willi syndrome also have a diagnosis of GHD, Norditropin is not indicated for the treatment of patients who have growth failure due to genetically confirmed Prader-Willi syndrome.

Blood glucose levels should be monitored periodically as treatment with somatropin may decrease insulin sensitivity. Patients with preexisting diabetes or glucose

intolerance should be monitored closely during somatropin therapy. Doses of insulin or oral agents may need to be adjusted for patients with diabetes on somatropin therapy.

Intracranial hypertension (IH) with papilledema, visual changes, headache, nausea and/or vomiting has been reported in a small number of patients treated with somatropin products. Symptoms usually occurred within the first eight (8) weeks after initiation of somatropin therapy and generally resolve after cessation of therapy or a reduction of the somatropin dose. Funduscopic examination should be performed routinely before initiating and periodically during the course of somatropin therapy. If papilledema is observed by funduscopy during somatropin treatment, treatment should be discontinued.

Pediatric patients may develop slipped capital femoral epiphyses more frequently if they have endocrine disorders or during rapid growth. Any child having onset of a limp or complaints of hip or knee pain during somatropin therapy should be carefully evaluated. Progression of scoliosis can occur in patients who experience rapid growth. Somatropin has not been shown to increase the occurrence of scoliosis.

In patients with GHD, central (secondary) hypothyroidism may first become evident or worsen during somatropin treatment. Patients treated with somatropin should therefore have periodic thyroid function tests and thyroid hormone replacement therapy should be initiated or adjusted as needed.

Somatropin inhibits 11 $\beta$ -hydroxysteroid dehydrogenase type 1 (11 $\beta$ HSD-1) in adipose/hepatic tissue, and may significantly impact the metabolism of cortisol and cortisone. In patients treated with somatropin, previously undiagnosed central (secondary) hypoadrenalism may be unmasked requiring glucocorticoid replacement therapy. In addition, patients treated with glucocorticoid replacement therapy especially with cortisone acetate and prednisone for previously diagnosed hypoadrenalism may require an increase in their maintenance or stress doses.

Careful monitoring is advisable when somatropin is administered in combination with other drugs known to be metabolized by CP450 liver enzymes (e.g., corticosteroids, sex steroids, anticonvulsants, cyclosporine) or other hormone replacement therapy.

The safety and effectiveness of Norditropin in patients age 65 years and older has not been evaluated in clinical studies. Elderly patients may be more sensitive to the actions of somatropin and may be more prone to develop adverse reactions.

Common somatropin-related adverse reactions include injection site reactions/rashes, lipoatrophy and headaches, glucose intolerance, fluid retention and unmasking of latent central hypothyroidism.

Most serious adverse reactions include intracranial hypertension, diabetic retinopathy, glucose intolerance, slipped capital femoral epiphysis, progression of preexisting scoliosis, sudden death in pediatric patients with Prader-Willi syndrome with risk factors including severe obesity, history of upper airway obstruction or sleep apnea and unidentified respiratory infection, intracranial tumors,

For prescribing information, please visit [norditropin-us.com](http://norditropin-us.com).

**About Novo Nordisk**

*Novo Nordisk is a healthcare company and a world leader in diabetes care. The company has the broadest diabetes product portfolio in the industry, including the most advanced products within the area of insulin delivery systems. In addition, Novo Nordisk has a leading position within areas such as hemostasis management, growth hormone therapy and hormone replacement therapy. Novo Nordisk manufactures and markets pharmaceutical products and services that make a significant difference to patients, the medical profession and society. With headquarters in Denmark, Novo Nordisk employs more than 22,750 employees in 79 countries, and markets its products in 179 countries. For more information, please visit <http://novonordisk-us.com>.*

<b>Media</b>	<b>Investors</b>
An Phan Novo Nordisk PH: (609) 987-4893	Christian Ovist Frandsen Novo Nordisk Tel: (609) 919-7937

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