6 February 2023

IMPORTANT PRESCRIPTION INFORMATION

Recommendation for switching patients treated with Norditropin NordiFlex® (somatropin, hormone of human growth) to alternative medicinal products due to a product shortage.

Direct communication to healthcare professionals

Dear Healthcare Professional,

Hereby as formal notification that the Norditropin NordiFlex® 15mg/1.5ml product will undergo a period of shortage from 15th April 2023, as Novo Nordisk is facing some production difficulties which will affect supplies of the afore mentioned medicinal product globally. This deficiency is not due to problems of safety or quality and has already been communicated to the Regulatory Authority in accordance with current legislation. Novo Nordisk SpA - via Elio Vittorini 129, 00144 Rome, Italy - on behalf of Novo Nordisk AS - would like to inform you of the following:

Summary and background information

Norditropin NordiFlex® contains somatropin which is a biosynthetic human growth hormone approved for use in several growth hormone related disorders [1] including:

Children:

• Short stature due to growth hormone deficiency (GHD)

• Short stature in girls due to gonadal dysgenesis (Turner syndrome)

• Growth retardation in prepubertal subjects associated with chronic renal failure

• Height deficit (current height SDS <-2.5 and height corrected on the basis of the average height of the parents SDS <-1) in children of short stature born small for gestational age (SGA) with birth weight and/or length less than - 2 SD, which have not shown growth recovery in the first 4 years or later (HV SDS<0 in the last year).

• Short stature due to Noonan Syndrome.

Adults:

• Childhood-onset growth hormone insufficiency:

Patients with pediatric onset GHD should be reassessed for secretory capacity for growth hormone after reaching full height. Re-evaluation is not required for those patients with a

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deficiency of more than three pituitary hormones, with severe GHD caused by a genetic mutation defined by structural hypothalamic pituitary abnormalities, central nervous system tumors, or high-dose irradiation of the skull, or with GHD secondary to hypothalamic-pituitary pathology or trauma, if levels serum insulin-like growth factor-1 (IGF-1) are <-2 SDS at least 4 weeks after discontinuation of growth hormone treatment.

In all other patients, IGF-1 measurement and a growth hormone stimulation test are required.

• Adult-onset growth hormone insufficiency:

Severe GHD in a person with known hypothalamic-pituitary disease, cranial irradiation, and traumatic brain injury. GHD must be associated with the deficiency of other axis except the prolactin axis. GHD must be demonstrated with a provocative stimulus test after the establishment of adequate replacement therapy for the deficits of each other axis.

The first-choice stimulus test in adults is the insulin tolerance test. When the insulin tolerance test is contraindicated, alternative stimulus tests should be used. Arginine hormone combination test is recommended of growth hormone releasing (GHRH). A stimulus test may also be considered with arginine or glucagon; however, these tests have less diagnostic value than the tolerance test insulin.

The product comes as a solution for injection in a pack of 1 pre-filled pen (AIC 027686118) with the following description:

Norditropin NordiFlex®15 mg/1.5ml 1 ml solution containing 10 mg of somatropin.

Out-of-stock situation will result in shortage of the medicine which may lead to a suboptimal treatment of patients.

Healthcare professionals are advised to ensure that patients using Norditropin NordiFlex® are informed of this problem and to safely switch patients to an alternative growth hormone therapy at their discretion, based on their clinical judgment and any relevant local regulations and/or guidelines institutional and professional.

- Novo Nordisk expects the medicine to be available again from February 2024.
- Novo Nordisk recognises the uncertainty and concern this event may cause to people with growth disturbances and their caregivers. We sincerely apologize for the disruption and the inconvenience this may cause.

Mitigating actions:

Physicians are advised to use locally approved and marketed alternatives to Norditropin NordiFlex®. The transition from one type of medicine to another should only be done in consultation with a doctor and requires strict medical supervision along with requirements in the prescribing information.

Physicians are advised not to initiate new patients on Norditropin NordiFlex® therapy.

Novo Nordisk is committed to ensuring continuity of care in patients with Short Stature due to Noonan Syndrome, for which there are no medicines authorized in Italy; for this purpose, based on consumption over the past years, the marketing authorization holder will reserve a dedicated stock of the medicinal product for these patients, to guarantee the therapeutic continuity even in the period of deficiency. For other indications, healthcare professionals are advised to follow their clinical judgment, relevant local regulations, and/or institutional and professional guidelines to regarding priorities in case of shortage.

More information and recommendations

Substitution with locally approved alternative possible:

- Main risk from a safety point of view is represented by the change of device.
- Available literature on the possible consequences of switching medicines during treatment with recombinant human growth hormone reports concerns about dosing errors and treatment interruptions due to the need to learn how to use a new device and reduced adherence related to patient's family frustration and anxiety [2].
- To mitigate the above risks, additional guidance is needed for patients until they can adequately handle their new device.

Reporting of adverse events

Adverse events including medication errors related to Norditropin NordiFlex® must be reported to the Italian Medicines Agency via the following link https://www.aifa.gov.it/web/guest/content/segnalazioni-reazioni-avverse and to Novo Nordisk SpA.

AIFA takes this opportunity to remind all Healthcare Professionals of the importance of reporting suspected adverse drug reactions, as an indispensable tool for confirming a report favourable risk benefit under real conditions of use. Reports of Suspected Adverse Reactions from drugs must be sent to the Head of Pharmacovigilance of the relevant Structure by the operator himself. This Information Note is also published on the AIFA website (www.agenziafarmaco.it) whose regular consultation is recommended for the best information to professional and citizen service.

References:

1. Norditropin® NordiFlex ® (somatropina) Riassunto delle Caratteristiche del Prodotto. Gennaio 2023

2. Grimberg A et al Endocr Pract. 2012 May-Jun;18(3):307-16. doi: 10.4158/EP11217.OR. PMID: 21940275.

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