Date: 22 March 2024

DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION

Norditropin NordiFlex® (somatropin): Product Discontinuation
Norditropin® FlexPro® 5mg/1.5ml (somatropin): Drug Shortage and Pause in production

Dear Healthcare Professional,

Novo Nordisk UK in agreement with the Medicines and Healthcare products Regulatory Agency (MHRA) and the Department of Health and Social Care (DHSC) would like to inform you of the following:

Due to a drug shortage for Norditropin, Novo Nordisk has decided to:

- **discontinue the production of Norditropin NordiFlex 5mg/1.5ml, 10mg/1.5ml and 15mg/1.5 ml immediately and permanently**

- **pause production of Norditropin FlexPro 5mg/1.5ml ONLY to assist with establishing a more consistent supply of Norditropin FlexPro 10mg/1.5ml and Norditropin FlexPro 15mg/1.5ml.**

Please refer to the Medicines Supply tool (SPS) for up to date information and advice from the DHSC.

Summary

- Novo Nordisk has two products which contain Norditropin – Norditropin NordiFlex and Norditropin FlexPro.
- It has been decided to discontinue the production of Norditropin NordiFlex 5mg/1.5ml, 10mg/1.5ml and 15mg/1.5ml immediately and permanently.
- Since late 2022, Novo Nordisk has experienced supply shortages with Norditropin NordiFlex. It has been in very limited supply since then. Despite all our efforts we were unable to ensure a consistent supply of Norditropin NordiFlex as we had planned.
- The immediate discontinuation of Norditropin NordiFlex will make more Norditropin available to support Norditropin FlexPro production.
- Norditropin FlexPro has had ongoing intermittent supply shortages throughout 2023 and into 2024.
- To re-establish a dependable supply for Norditropin FlexPro Novo Nordisk has decided to **temporarily pause** the production of Norditropin FlexPro 5mg/1.5ml ONLY. Stock already produced for the UK will continue to be made available – please refer to the Medicines Supply tool (SPS) for further information.
- Pausing production of Norditropin FlexPro 5mg/1.5ml will help to ensure a more consistent supply of higher doses of Norditropin FlexPro (10mg/1.5ml and 15mg/1.5ml), therefore allowing continuity of supply for as many patients as possible.
- These decisions are not a consequence of any safety or quality related issues.
- Refer to the Medicines Supply tool (SPS) for the most up to date information, stock information and advice from the DHSC.

Further information on Norditropin NordiFlex (5mg/1.5ml, 10mg/1.5ml and 15mg/1.5ml) and Norditropin FlexPro (5mg/1.5ml)

- Ensure that new patients are not initiated on Norditropin NordiFlex or Norditropin FlexPro.
- Healthcare professionals (HCPs) are urged to ensure that patients are safely switched to an alternative growth hormone treatment as per the prescribers' clinical discretion. Additional guidance and support should be provided to patients and caregivers until they are comfortable with the alternative product supplied to them.
- Delayed action to support patients to change to an alternative treatment, where required, could have clinical consequences for the patient.
- Notify patients who are currently using Norditropin NordiFlex and Norditropin FlexPro 5mg/1.5ml.
- Remind your colleagues of these actions, particularly if they are known to use/prescribe Norditropin.

- Norditropin NordiFlex and Norditropin FlexPro contain somatropin which is a biosynthetic human growth hormone used in several growth hormone related disorders. It is a solution for injection in a pre-filled pen 5mg/1.5ml, 10mg/1.5ml and 15mg/1.5ml.
- Norditropin NordiFlex and Norditropin FlexPro are indicated:
  In Children: Growth failure due to growth hormone deficiency (GHD), Growth failure in girls due to gonadal dysgenesis (Turner syndrome), Growth retardation in prepubertal children due to chronic renal disease, Growth disturbance (current height SDS < -2.5 and parental adjusted height SDS < -1) in short children born small for gestational age (SGA), with a birth weight and/or length below -2 SD, who failed to show catch-up growth (HV SDS < 0 during the last year) by 4 years of age or later, and Growth failure due to Noonan syndrome.
  In Adults: Childhood onset growth hormone deficiency: Patients with childhood onset GHD should be re-evaluated for growth hormone secretory capacity after growth completion. Testing is not required for those with more than three pituitary hormone deficits, with severe GHD due to a defined genetic cause, due to structural hypothalamic pituitary abnormalities, due to central nervous system tumours or due to high-dose cranial irradiation, or with GHD secondary to a pituitary/hypothalamic disease or insult, if measurements of serum insulin-like growth factor 1 (IGF-1) is < -2 SDS after at least four weeks off growth hormone treatment. In all other patients an IGF-1 measurement and one growth hormone stimulation test is required.
  Adult-onset growth hormone deficiency: Pronounced GHD in known hypothalamic-pituitary disease, cranial irradiation, and traumatic brain injury. GHD should be associated with one other deficient axis, other than prolactin. GHD should be demonstrated by one provocative test after institution of adequate replacement therapy for any other deficient axis.

Background on the safety concern

Please refer to the Summary of Product Characteristics (SmPC) for the details of therapeutic indication:

- Norditropin emc link[2]: https://www.medicines.org.uk/emc/search?q=Norditropin

Information and advice is issued by the DHSC. This is available on Medicine Supply Tool within the Specialist Pharmacy Service website. You may need to register to access the Medicine Supply Tool (www.sps.nhs.uk/wp-login.php).

Advice for Healthcare Professionals

- You are advised to use approved alternatives to Norditropin NordiFlex and Norditropin FlexPro 5mg/1.5ml. Support patients to change to an alternative treatment. Switching requires strict medical supervision by an endocrine specialist along with any prescribing requirements as stated in the relevant SmPC.

Further information on recommendations to healthcare professionals - Substitution with approved alternative treatment

The primary risk from a safety perspective are the challenges related to switching device. Please do bear in mind that the available literature on possible consequences of switching brand during recombinant human growth hormone treatment includes concerns involving dosing errors and treatment lapses from having to learn how to use a new device and impaired adherence related to patient-family frustration and anxiety.[1]
To mitigate the above risks, additional guidance and support should be provided to patients and caregivers until they are comfortable with the alternative product supplied to them.

Please ensure all relevant staff are made aware of the content of this letter and that the information is communicated to patients.

Call for reporting

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme.
Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle ▼.

Healthcare professionals are asked to report any suspected adverse reactions to the Yellow Card scheme.

You can report via:

- The Yellow Card website - https://yellowcard.mhra.gov.uk/
- The free Yellow Card app available from the Apple App Store or Google Play Store
- Some clinical IT systems (EMIS, SystmOne, Vision, MiDatabank) for healthcare professionals

Alternatively, you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset timing, treatment dates, and product brand name.

The non-identical nature of biological medicines and vaccines means it is very important that safety surveillance is carried out on a brand/product-specific basis. When reporting a suspected ADR to a biological medicine (such as blood products, antibodies and advanced therapies [such as gene and tissue therapy]) or vaccine, please ensure that you provide the brand name (or product licence number and manufacturer), and the specific batch-number. Additionally, when providing patients with details of the vaccine or biological medicine administered, it is good practice to give them details of the brand and batch number. This will allow patients and carers to report suspected ADRs more accurately to the Yellow Card scheme.

Company contact point

If you have any questions about this letter or require more information, please contact Novo Nordisk Customer Care Centre on 0800 023 2573.

Yours sincerely,

Dr Avideh Nazeri
Vice President, Clinical Development, Medical and Regulatory Affairs (CMR), Novo Nordisk UK

References

1. Grimberg A et al Endocr Pract. 2012 May-Jun;18(3):307-16. doi: 10.4158/EP11217.OR. PMID: 21940275.
2. Norditropin emc link: https://www.medicines.org.uk/emc/search?q=Norditropin