Medicine Shortage Communication

<Date>

Marketing cessation (discontinuation) of selected presentations of

- **short- and rapid-acting (bolus/mealtime) insulins (human insulin, 100 units/ml, solution for injection)**
- **intermediate-acting (isophane) insulins (NPH human insulin, 100 units/ml, solution for injection)**
- **mixed-acting (biphasic) insulins (suspension for injection)**
- **long-acting (basal) insulins (solution for injection in pre-filled pen)**

Dear Healthcare Professional,

Novo Nordisk A/S [affiliate to include country specific information to reflect global or local company name] is notifying healthcare professionals about the discontinuation of the following presentations of its insulin formulations in <Member State>. These presentations will be discontinued across all EU/EEA countries where they are marketed.

Products	Presentation(s) subject to marketing cessation (discontinuation)	Presentation(s) remaining available
Short- and rapid-acting insulins		
<Actrapid (regular human insulin, 100 units/ml, solution for injection)>	<Penfill > <Flexpen> <Innolet>	<Vial> <None>
<Fiasp (fast-acting insulin aspart, 100 units/ml, solution for injection)>	<Pumpcart>	<Flextouch> <Vial> <Penfill> <None>
Intermediate-acting insulins		
<Insulatard (insulin NPH, 100 units/ml, suspension for injection in cartridge)>	<Penfill> <Innolet> <Flexpen>	<Vial> <None>
<Protaphane (isophane/NPH human insulin, 100 units/ml, suspension for injection in cartridge)>	<Penfill> <Flexpen>	<Vial> <None>
Mixed-acting (biphasic) insulins		
<Mixtard 30 (30% soluble insulin and 70% isophane insulin, 100 units/ml, suspension for injection in cartridge or pre-filled pen)>	<Penfill> <Innolet> <Flexpen>	<Vial)> <None>
<Mixtard 50 (50% soluble insulin and 50% isophane	<Penfill>	<None>

Products	Presentation(s) subject to marketing cessation (discontinuation)	Presentation(s) remaining available
insulin, 100 units/ml, suspension for injection in cartridge or pre-filled pen)>		
<Actraphane 30 (30% soluble insulin and 70% isophane insulin, 100 units/ml, suspension for injection in cartridge or pre-filled pen)>	<Penfill> <Flexpen>	<Vial> <None>
<Actraphane 50 (50% soluble insulin and 50% isophane insulin, 100 units/ml, suspension for injection in cartridge or pre-filled pen)>	<Penfill > <Flexpen >	<None>
<NovoMix 50 (50% insulin aspart and 50% insulin aspart protamine 100 units/ml, suspension for injection in cartridge or pre-filled pen)>	<Penfill> <Flexpen>	<None>
Long-acting insulins		
<Levemir (insulin detemir 100 units/ml, solution for injection, in cartridge or pre-filled pen)>	<Penfill> <Flexpen> <Innolet> <Flextouch>	<None>

<**Note**: Angular brackets (<>) are used to allow flexibility for accurately reflecting the respective national situation (taking into account that listed presentations/products are not marketed in all EU/EEA countries). The bracketed text should be removed based on which presentations are currently marketed and will be discontinued in the respective country.>

<In addition, Novo Nordisk will discontinue the following insulin presentations in <Member State>. These are not EU/EEA-wide discontinuations and only affect selected Member States.>

The presentations currently in scope are listed in the Appendix. In the national version of the MSC these national discontinuations must be shown in a separate table within this section. Please update the Appendix Table and move it here, so that HCPs also have a clear overview of the national discontinuations in their country.

Overview of situation

- **Novo Nordisk will discontinue the above listed presentations of insulins in <Member State>.**

The discontinuation is not a consequence of any safety or quality related issue.

Mitigation measures

In order to manage the discontinuation, Novo Nordisk is engaging with the European Medicines Agency and the [National Competent Authority] on mitigation measures.

Regulatory authorities, physicians, healthcare providers, and patient organisations are being informed to help patients safely transition to alternative options for continuity of care.

Patients need to be switched to an alternative insulin treatment in time to avoid the risk of missing doses of insulin, which may lead to serious clinical consequences.

Healthcare professionals (HCPs) should consider the following mitigation measures:

- No new patients should be started on the above listed insulins.
- **Short- and rapid-acting insulins:** Healthcare professionals should switch any patients who are currently on any of the listed insulins to alternative insulins (such as insulin aspart or its biosimilars, insulin lispro or its biosimilars, or insulin glulisine or its biosimilars) based on existing guidance and clinical judgment.
- **Intermediate-acting insulins**: Healthcare professionals should switch any patients who are currently on any of the listed insulins to alternative insulins based on existing guidance and clinical judgment.
- **Mixed-acting (biphasic) insulins:** Healthcare professionals should switch patients who are currently on any of the above listed insulins to an alternative mixed insulin preparation or basal-bolus therapy or their biosimilars, based on existing guidance and clinical judgment.
- **Long-acting insulins:** Healthcare professionals should switch any patients who are currently on any of the above listed long-acting insulins to an alternative once-daily or once-weekly basal insulin preparation or their biosimilars.

In addition:

- Healthcare professionals should ensure that all patients are counselled on any changes in the new insulin regimen and/or usage of the new insulin delivery system. This includes a potential need for change in dose and additional glucose monitoring.
- Close glucose monitoring is recommended during the transfer to another type or brand of insulin and in the initial weeks thereafter, especially in pregnant women and children who may need closer monitoring than the general population. The risk of hypoglycaemia may be higher in these populations.
- Healthcare professionals should follow the relevant product SmPCs for dosing recommendations while switching patients to alternative insulin products.

Note:

When switching to an alternative insulin, healthcare professionals may need to adjust the dose due to potential differences in the pharmacokinetics/pharmacodynamics (PK/PD), efficacy and safety profiles between the new insulin and the one being replaced. The dose may need to be adjusted immediately before or after the switch. However, the need for dose adjustment may also only be required several weeks after the switch and may also affect the basal or bolus insulin requirement (if the patient is on basal-bolus regimen) or anti-diabetic medication that the patient may be taking.

Background information

- **Short- and rapid-acting (bolus/mealtime) insulins** are a type of fast-acting insulin analogue used to manage blood sugar levels, particularly after meals. They start working quickly, typically within 15 minutes, and their effects last for a shorter duration, around 2 to 4 hours. Common examples include insulin lispro, insulin aspart, and insulin glulisine. They are usually taken immediately before or shortly after meals to control mealtime glucose spikes. [affiliate to include country specific **indication** information]. [affiliate to include country specific **presentation** information].
- **Intermediate-acting (isophane/NPH) insulins** are a type of insulin that have a longer duration of action compared to short-acting insulins, helping to manage blood sugar levels over a more extended period. These insulins typically start working within 1-2 hours after injection, peak in 4-6

hours, and can last for up to 12-24 hours. They are usually taken once or twice daily, commonly in the morning and/or evening to maintain basal insulin levels throughout the day and night. [affiliate to include country specific **indication** information]. [affiliate to include country specific **presentation** information].

- **Mixed-acting (biphasic) insulins** combine rapid- or short-acting insulin with intermediate-acting or long-acting insulin in a single injection. This provides both immediate and longer-lasting coverage for managing blood glucose levels, mimicking the body's natural insulin response to meals and basal needs. Mixed-acting (biphasic) insulins start to work within 30 minutes and last for up to 24 hours. They are usually taken twice a day, before breakfast and the evening meal. [affiliate to include country specific **indication and presentation** information]. **Long-acting (basal) insulins** start to work after 30 minutes to 4 hours, depending on the type. Their action usually lasts for 16 to 24 hours, depending on the type and dose. They are usually taken once or twice a day. [affiliate to include country specific **indication and presentation** information].

Healthcare professionals should refer to the relevant SmPC for more information.

Safety instructions and general information

A delay in switching to an alternative insulin treatment could result in patients missing their required doses, which may lead to serious clinical consequences.

When changing patients' insulin therapy, the following should be taken into account:

- Switching a patient to a different type and/or brand of insulin must be carried out under medical supervision.
- A change in insulin therapy can lead to an unstable metabolic situation. In turn, this can lead to impairments in the patient's daily life (e.g., driving a motor vehicle) and must be discussed with the patient.
- Switching to an alternative insulin requires close monitoring of blood glucose (including nightly measurements if necessary) during the switching process and in the first few weeks afterwards.
- Patients may require training when switching to a new presentation/delivery system.

Note:

When switching patients from one insulin preparation to an alternative, the changes in the PK/PD, efficacy and safety profiles of the insulin analogues must be taken into account and the patient should be trained accordingly.

Company contact point

Further information can be obtained by contacting <local Novo Nordisk affiliate contact details to be added by affiliate>

Yours Sincerely,

Medical Director

<Appendix

The below presentations are subject to selected national discontinuations in one or more EU/EEA countries. Please update the table below and move it into the main text, so that HCPs have a clear overview of the national discontinuations in your country.

Products	Presentation(s) subject to national marketing cessation (discontinuation)	Presentation(s) remaining available
Short- and rapid-acting insulins		
<Fiasp (fast-acting insulin aspart, 100 units/ml, solution for injection)>	<Flextouch> <Vial>	<Flextouch> <Vial> <Penfill> <None>
<NovoRapid (insulin aspart, 100 units/ml, solution for injection)>	< Vial> <Pumpcart> <Penfill> <Flexpen>	< Vial> <Pumpcart> <Penfill> <Flexpen> <None>
Mixed-acting (biphasic) insulins		
<NovoMix 30 (30% insulin aspart and 70% insulin aspart protamine, 100 units/ml, suspension for injection)>	<Penfill> <Flexpen>	<None> <Penfill> <Flexpen>
<Ryzodeg (insulin degludec and insulin aspart, 100 units/mL solution for injection in pre-filled pen)>	<Flextouch>	<None>
Long-acting insulins		
<Tresiba (insulin degludec <100 units/ml> <and> <200 units/ml>, solution for injection, in prefilled pen)>	<Flextouch>	<Flextouch> <Flexpen> <None>

Note: Angular brackets in the text are used to allow flexibility for accurately reflecting national situation (taking into account that listed presentations/products are not marketed in all EU/EEA). The bracketed text should be updated or removed based on which presentations are currently marketed and will be discontinued in the country.

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Communication Plan for Medicine Shortage Communication

MSC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	**Presentations to be discontinued across all EU/EEA countries:** - Short- and rapid-acting insulins <Actrapid [<Penfill,> <FlexPen,> <Innolet>] [Human Insulin]> <Fiasp [<PumpCart>] [Aspart Insulin]> - Intermediate-acting insulins <Insulatard [<Penfill,> <Innolet,> <Flexpen>] [NPH insulin]> <Protaphane [<Penfill,> <Flexpen>] [isophane/NPH human insulin]> - Mixed-acting (biphasic) insulins <Mixtard 30 [<Penfill,> <Innolet,> <Flexpen>] [30% soluble insulin and 70% isophane insulin]> <Mixtard 50 [<Penfill>] [50% soluble insulin and 50% isophane insulin]> <Actraphane 30 [<Penfill,> <Flexpen>] [30% soluble insulin and 70% isophane insulin]> <Actraphane 50 [<Penfill,> <Flexpen>] [50% soluble insulin and 50% isophane insulin]> <Novomix 50 [<Penfill,> <Flexpen>] [50% insulin aspart and 50% insulin aspart protamine]> - Long-acting insulins <Levemir [Penfill,> <Innolet,> <Flextouch>] [insulin detemir]> **Presentations currently subject to only national discontinuation in one or more EU/EEA countries:** - Short- and rapid-acting insulins <Fiasp [<Flextouch,> <Vial>] [Aspart Insulin]> <NovoRapid [<Vial,> <Penfill,> <FlexPen>] [Aspart Insulin]> - Mixed-acting (biphasic) insulins <Novomix 30 [<Penfill,> <Flexpen>]> [30% insulin aspart and 70% insulin aspart protamine] <Ryzodeg [<Flextouch>] [insulin degludec and insulin aspart]> - Long-acting insulins <Tresiba [<Flextouch>] [insulin degludec]>

MSC COMMUNICATION PLAN	
Marketing authorisation holder(s)	Novo Nordisk A/S
Purpose of the communication	Inform Healthcare Professionals on discontinuations of selected insulins and measures to take.
MSC recipients	Target group for this letter is specialists that treat patients with diabetes (e.g. endocrinologists, diabetologists, specialists in internal medicine, general practitioners /family physicians, pharmacists, diabetes nurses) in all EU/EEA countries in which the medicinal products are marketed. The target group can be further defined at national level, in agreement with the respective national competent authorities.
Member States where the MSC will be distributed	In agreement with the national competent authorities.

Timetable *[Delete steps which are not applicable]*	**Date**
MSC and communication plan (in English) agreed by SPOC WP	26/09/2025
MSC and communication plan (in English) agreed by MSSG	06/10/2025
Submission of translated MSCs to the national competent authorities for review	14/10/2025
Agreement of translations by national competent authorities	21/10/2025
Dissemination of MSC	In consultation with the NCAs