Date: 04 Aug 2025

**DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION**

# Rybelsus® (oral semaglutide): risk of medication error due to introduction of new formulation with increased bioavailability

Dear Healthcare Professional,

Novo Nordisk UK would like to inform you of the following:

## Summary

- **Rybelsus tablets will be replaced with a new formulation with increased bioavailability, which is bioequivalent to the initial formulation as described in the table below:**

| Initial formulation (one oval tablet) | Bioequivalent | New formulation (one round tablet) |
|---|---|---|
| **3 mg (starting dose)** | **=** | **1.5 mg (starting dose)** |
| **7 mg (maintenance dose)** | **=** | **4 mg (maintenance dose)** |
| **14 mg (maintenance dose)** | **=** | **9 mg (maintenance dose)** |

- **The new formulation has the same efficacy, safety and method of administration as the initial formulation.**
- **Rybelsus should always be used as one tablet per day.**
- **The two formulations will temporarily co-exist on the market, which may cause mix-ups. This could result in overdosing, which increases the risk of adverse events.**
- **Patients currently taking Rybelsus should be informed and advised about the change in formulation and dose when the new formulation is prescribed or dispensed.**
- **Patients starting Rybelsus treatment should be prescribed the new formulation and be suitably informed by the prescriber or pharmacist.**

### Background on the safety concern

Rybelsus is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise.

Novo Nordisk is replacing the initial formulation (3 mg, 7 mg, 14 mg tablets) of Rybelsus with the new formulation (1.5 mg, 4 mg, 9 mg tablets).

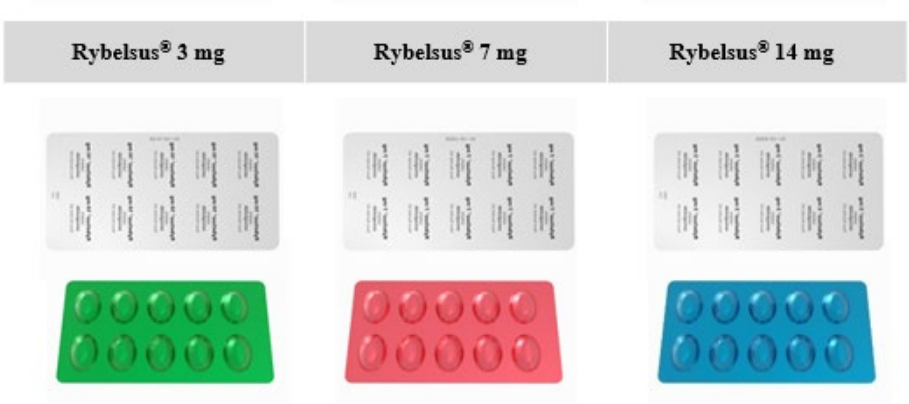
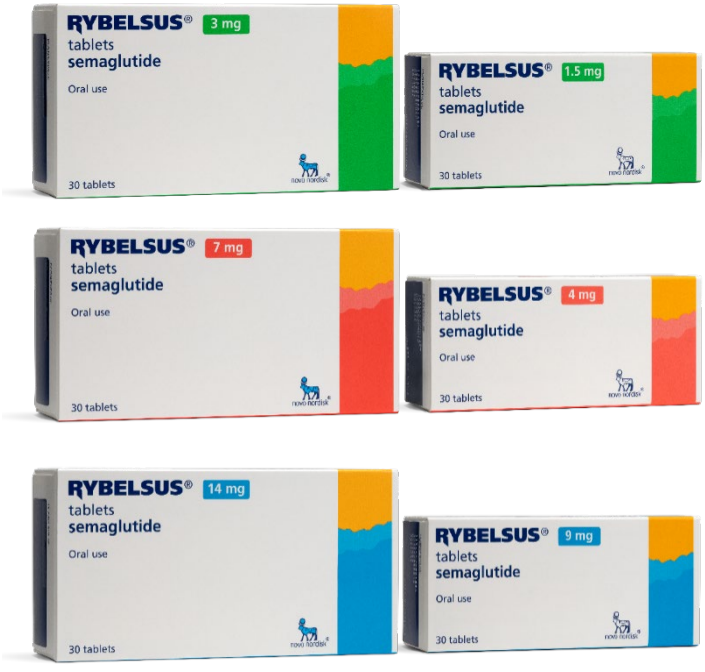
In comparison with the initial formulation, the excipients in the new formulation have been modified to increase absorption. The new formulation has increased bioavailability resulting in lower doses to attain the same drug exposure. Bioequivalence has been shown in a clinical trial and the doses of the new formulation have the same efficacy and safety as the initial formulation. This means that the data generated in the phase 3 clinical trial programme of Rybelsus is applicable to the new formulation. This allows switching between corresponding doses of the initial formulation and the new formulation. The method of administration remains the same.

The co-existence of both formulations during the transition period could potentially lead to confusion and pose a risk of medication errors. Medication errors could result in increased exposure of semaglutide, which could lead to gastrointestinal adverse events e.g. nausea, vomiting and diarrhoea.

The Product Information has been updated to explain the difference between the two formulations and enable readers to identify the equivalent doses across formulations with bioequivalent doses.
Please refer to the Rybelsus SmPC: http://www.medicines.org.uk/emc/search?q=rybelsus

The packaging and tablet shape for the new formulation differ from the initial formulation, but the colour of the different dosing steps has been kept similar. See tables below.

| | |
|---|---|
| **Tablet size:** Tablets for the new formulation are smaller in size and have a different shape (round). Tablets are debossed with strength. | **Initial** **New**   |

| | |
|---|---|
| **Primary packaging: New formulation blisters are silver both on the front and back and are smaller compared to blisters with the initial formulation** | **Initial formulation**<br>  <br>**New formulation**<br>  |
| **Secondary packaging: Cartons for the new formulation are smaller** | **Initial formulation carton** **New formulation carton**<br>  |

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

**Call for reporting**

Healthcare professionals are asked to report any suspected adverse drug reactions (ADRs) including medication errors 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 more accurately report suspected ADRs 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,

Avideh Nazeri

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