DIRECT HEALTHCARE PROFESSIONAL COMMUNICATION AND COMMUNICATION PLAN

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

Dear Healthcare professional,

Novo Nordisk A/S [affiliate to include country specific information to reflect global or local company name] in agreement with the European Medicines Agency and the <National Competent Authority > 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.

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 table below.

<table>
<tr>
<td>Tablet size: Tablets for the new formulation are smaller in size and have a different shape (round). Tablets are debossed with strength.</td>
<td>Initial New
 
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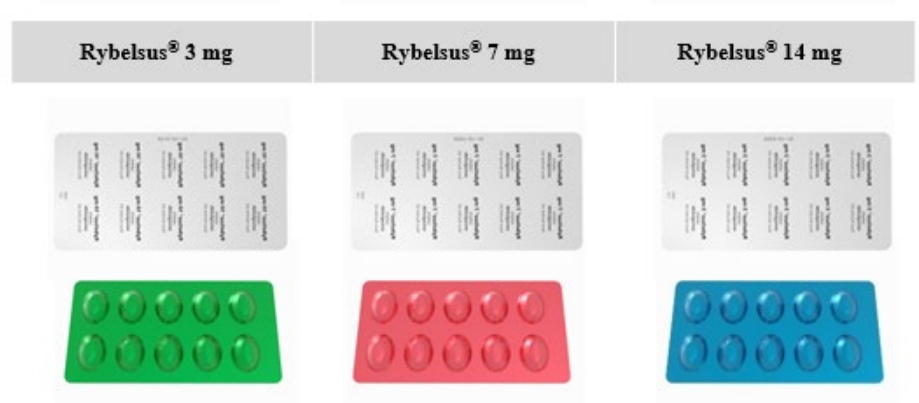
<tr>
<td>Primary packaging: New formulation blisters are silver both on the front and back and are smaller compared to blisters with the initial formulation</td>
<td>Initial formulation
 

New formulation
 
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</table>

Secondary packaging: Cartons for the new formulation are smaller	**Initial formulation carton** **New formulation carton** 

Call for reporting

Adverse reactions including medication errors relating to Rybelsus should be reported in accordance with the national spontaneous reporting system <include the details (e.g. name, postal address, fax number, website address) on how to access the national spontaneous reporting system>.

Company contact point

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

DHPC COMMUNICATION PLAN	
Medicinal product(s)/active substance(s)	Rybelsus (oral semaglutide) tablets
Marketing authorisation holder(s)	Novo Nordisk A/S
Safety concern and purpose of the communication	The purpose of the communication is to notify healthcare professionals (HCPs) of a change in formulation of Rybelsus. The two formulations will temporarily co-exist on the market which could lead to mix-ups between the formulations and to potential medication errors.
DHPC recipients	Target group for this letter are prescribing HCPs that treat patients with diabetes and pharmacists. Depending on national health care systems it may additionally be considered to add diabetic nurse practitioners and physician assistants. The target group should be further defined at national level, in agreement with the respective national competent authority
Member States where the DHPC will be distributed	All EU/EEA member states where the initial formulation of Rybelsus has been launched

Timetable	Date
DHPC and communication plan (in English) agreed by PRAC	11 April 2024
DHPC and communication plan (in English) agreed by CHMP	25 April 2024
Submission of translated DHPCs to the national competent authorities for review	02 May 2024
Agreement of translations by national competent authorities	13 May 2024
Dissemination of DHPC	To be determined – At launch date of the new formulation in the concerned MS