European Medicines Agency reviews the risk of suicidal thoughts with GLP-1 receptor agonists

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Information on glucagon-like peptide 1 (GLP-1) agonists

- Glucagon-like peptide 1 (GLP-1) agonists are a class of medicines that include dulaglutide, exenatide, liraglutide, lixisenatide and semaglutide.
- GLP-1 agonists work by activating the GLP-1 receptor in the pancreas. They slow gastric emptying, inhibit the release of glucagon, stimulate insulin production, and reduce hyperglycemia.
- These medicines are authorised under different trade names for treating type 2 diabetes (Rybelsus, Victoza, Bydureon, Lyxumia, Byetta, Ozempic, and Trulicity) and for weight loss (Wegovy and Saxenda)

In Malta the following products are available through centralised licensing procedures;

Active Ingredients	Product Name	Pharmaceutical Form	Classif-cation	Authorisation Number	MAH/license holder
Liraglutide	Victoza	Solution for injection in pre-filled pen	POM	EMEA/H/C/001026	Novo Nordisk A/S
Semaglutide	Ozempic	Solution for injection in pre-filled pen	POM	EMEA/H/C/004174	Novo Nordisk A/S
Dulaglutide	Trulicity	Solution for injection in pre-filled pen	POM	EMEA/H/C/002825	Eli Lilly Nederland B.V.

Information from the EMA about the safety concern

The European Medicines Agency's safety committee, the Pharmacovigilance Risk Assessment Committee (PRAC), is reviewing data on the risk of suicidal thoughts and thoughts of self-harm with medicines known as glucagon-like peptide (GLP-1) receptor agonists. The medicines include semaglutide (Wegovy, Rybelsus, Ozempic), liraglutide (Saxenda, Victoza), dulaglutide (Trulicity), exenatide (Bydureon, Byetta), and lixisenatide (Lyxumia). These medicines are authorised for type 2 diabetes (Rybelsus, Victoza, Xultophy, Bydureon, Lyxumia, Suliqua, Byetta, Ozempic, and Trulicity) and weight loss (Wegovy and Saxenda)

The review was triggered in July 2023 by the Icelandic Medicines Agency following reports of suicidal thoughts and self-injury in people using liraglutide and semaglutide medicines. At the

start of the review, about 150 reports of possible cases of self-injury and suicidal thoughts were retrieved and are currently being analysed.

Liraglutide and semaglutide medicines are widely used, with an exposure of over 20 million patient-years[1] to date. Saxenda (Liraglutide) and Wegovy (semaglutide) are authorised for weight management, together with diet and physical activity in people who are obese or overweight in the presence of at least one weight-related health problem. Ozempic (semaglutide) is authorised for the treatment of adults with insufficiently controlled type 2 diabetes as an adjunct to diet and exercise but has been used off-label for weight loss.

Suicidal behaviour is not currently listed as a side effect in the EU product information for any GLP-1 receptor agonists. It is not yet clear whether the reported cases are linked to the medicines themselves or to the patients' underlying conditions or other factors.

The review is being carried out in the context of a signal procedure. A signal is information on a new adverse event that is potentially caused by a medicine or a new aspect of a known adverse event that warrants further investigation. The presence of a signal does not necessarily mean that a medicine caused the adverse event in question.

For more information please see the European Medicines Agency's press release

In Malta

For Healthcare Professionals

As with all medicines, healthcare professionals are advised to use GLP- 1 receptor agonists in accordance with the approved product information and/or local guidelines.

Product information for GLP - 1 receptor agonists is available on the EMA website (refer to Ozempic, Trulicity, Victoza)

The increased demand for Ozempic has led to intermittent shortages. For further information refer to previously published DHPCs (see Ozempic DHPC published on 13-10-2022 and Ozempic DHPC published on 06-03-2023).

Advice for Patients

Patients should not stop taking GLP-1 receptor agonists without first consulting their health care professional, as stopping these medicines may worsen their condition. Talk to your health care professional if you have questions or concerns. Tell your health care professional if you experience new or worsening depression, suicidal thoughts, or any unusual changes in mood or behaviour.

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[1] One patient-year is the equivalent of one patient taking a medicine for one year.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on GLP-1 receptor agonists containing medicinal products. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 or online to **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

Post-Licensing Directorate
Malta Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Malta Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Feedback Form

The Malta Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health

The Malta Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this formt (address side up), stapling the ends and then posting (no stamp required)

Feedback:

We thank you for your interest and look forward to hearing your opinion.

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Pharmacovigilance Section

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