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SCIENCE MEDICINES HEALTH

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News announcement

Meeting highlights from the Pharmacovigilance Risk Assessment Committee (PRAC) 23-26 October 2023

GLP-1 receptor agonists: available evidence not supporting link with thyroid cancer

EMA's safety committee (PRAC) has concluded that the available evidence does not support a causal association between the Glucagon-Like Peptide-1 Receptor Agonists (GLP-1) - exenatide, liraglutide, dulaglutide, semaglutide, and lixisenatide - and cancer of the thyroid (a small gland in the front and lower part of the neck which makes and releases hormones).

These medicines are used to treat type 2 diabetes and, in some cases, for the treatment of obesity under certain conditions. The PRAC began assessing this safety signal following the publication of a study[1] suggesting that there might be an increased risk of thyroid cancers with the use of these medicines in patients with type 2 diabetes mellitus.

The committee reviewed evidence from the published literature, including observational studies (Bezin et al, 2022; Alves et al, 2012: Hu et al, 2022; Bea et al, 2023) as well as cumulative data submitted by the marketing authorisation holders (MAHs) which included non-clinical, clinical and post-marketing data. At present, the PRAC considers that no updates to the product information are warranted based on the available data.

The MAHs for liraglutide- (including Victoza, Saxenda, Xultophy), semaglutide- (including Ozempic, Rybelsus, Wegovy), exenatide- (including Bydureon, Byetta), dulaglutide- (i.e.Trulicity) and lixisenatide- (including Lyxumia, Suliqua) containing products should continue to monitor these events

1 Bezin et al. GLP-1 Receptor Agonists and the Risk of Thyroid Cancer. Bezin et al. 2022 Diabetes Care. 2022 Nov 10; dc221148. doi: 10.2337/dc22-1148. (Online ahead of print)

2 Alves C, Batel-Marques F, Macedo AF. A meta-analysis of serious adverse events reported with exenatide and liraglutide: acute pancreatitis and cancer. Diabetes Res Clin Pract. 2012 Nov;98(2):271-84. doi: 10.1016/j.diabres.2012.09.008. Epub 2012 Sep 23. PMID: 23010561.

3 Hu W, Song R, Cheng R, Liu C, Guo R, Tang W, Zhang J, Zhao Q, Li X, Liu J. Use of GLP-1 Receptor Agonists and Occurrence of Thyroid Disorders: a Meta-Analysis of Randomized Controlled Trials. Front Endocrinol (Lausanne). 2022 Jul 11;13:927859. doi: 10.3389/fendo.2022.927859. PMID: 35898463; PMCID: PMC9309474.

4 Bea S, Son H, Bae JH, Cho SW, Shin JY, Cho YM. Risk of thyroid cancer associated with glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in patients with type 2 diabetes: A population-based cohort study. Diabetes Obes Metab. 2023 Sep 21. doi: 10.1111/dom.15292. Epub ahead of print. PMID: 37735822.

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closely, including any new publications, as part of their routine pharmacovigilance activities and report any new evidence on this issue in their Periodic Safety Update Reports (PSURs) submissions.

PRAC statistics: November 2023

[infographic]

Glossary:

- **Safety signal assessments**. A safety signal is information which suggests a new potentially causal association, or a new aspect of a known association between a medicine and an adverse event that warrants further investigation. Safety signals are generated from several sources such as spontaneous reports, clinical studies and the scientific literature. More information can be found under 'Signal management'.
- **Periodic safety update reports**, abbreviated as PSURs, are reports prepared by the marketing authorisation holder to describe the worldwide safety experience with a medicine in a defined period after its authorisation. PSURs for medicinal products that contain the same active substance or the same combination of active substances but have different marketing authorisations and are authorised in different EU Member States, are jointly assessed in a single assessment procedure. More information can be found under 'Periodic safety update reports: questions and answers'.
- **Risk management plans**, abbreviated as RMPs, are detailed descriptions of the activities and interventions designed to identify, characterise, prevent or minimise risks relating to medicines. Companies are required to submit an RMP to EMA when applying for a marketing authorisation. RMPs are continually updated throughout the lifetime of the medicine as new information becomes available. More information is available under 'Risk-management plans'.
- **Post-authorisation safety studies**, abbreviated as PASSs, are studies carried out after a medicine has been authorised to obtain further information on its safety, or to measure the effectiveness of risk-management measures. The PRAC assesses the protocols (aspects related to the organisation of a study) and the results of PASSs. More information can be found under 'Post-authorisation safety studies'.
- **Referrals** are procedures used to resolve issues such as concerns over the safety or benefit-risk balance of a medicine or a class of medicines. In a referral related to safety of medicines, the PRAC is requested by a Member State or the European Commission to conduct a scientific assessment of a particular medicine or class of medicines on behalf of the EU. More information can be found under referral procedures.
- **Summary safety reports** have been introduced as part of the enhanced safety monitoring of COVID-19 vaccines. Marketing authorisation holders are required to submit these reports to EMA, starting on a monthly basis. Their submission complements the submission of PSURs. For more information see EMA's pharmacovigilance plan for COVID-19 vaccines.

Ongoing referrals

Procedure	Status	Update
Pseudoephedrine-containing medicinal products - Article-31 referral	Under evaluation	PRAC continued its assessment.
Hydroxyprogesterone-containing medicinal products – Article-31 referral	Under evaluation	PRAC continued its assessment.