BRITISH GENERIC MANUFACTURERS ASSOCIATION

May 2023

Levothyroxine containing products: Biotin interference with laboratory tests – Important Safety Information.

Dear Healthcare Professional,

The marketing authorisation holders of levothyroxine, Glenmark Pharmaceuticals Limited, Accord Healthcare Ltd, TEVA UK Ltd, Advanz Pharma, Zentiva Pharma UK Limited and Wockhardt UK Limited in agreement with the European Medicines Agency and the MHRA, would like to inform you of the following:

Summary

- **Biotin may interfere with thyroid immunoassays that are based on a biotin/streptavidin interaction.**
- **These test methods are commonly used in clinical practice for the measurement of thyroid function tests and therapeutic drug monitoring for the adjustment of levothyroxine dosage.**
- **Depending on the assay design, test results may be falsely increased or falsely decreased. This may lead to inappropriate patient management or misdiagnosis.**
- **If results of thyroid function tests do not match the clinical presentation and/or other investigations, the possibility of biotin interference should be taken into consideration.**
- **Patients should be routinely asked about biotin use before ordering thyroid function tests. If a patient is taking biotin, inform the laboratory personnel before ordering the tests, alternative assays might be available.**
- **Patients should be advised to consult their doctor if they are taking or have recently taken biotin. They should also be made aware that, other products that they may take, such as multivitamins or supplements for hair, skin, and nails could also contain biotin and affect the results of their thyroid function tests.**

Background on the safety concern

Levothyroxine is a synthetic thyroid hormone that is authorised in adults and children for the treatment of a number of conditions associated with hypothyroidism, as well as in suppression therapy for thyroid carcinoma and for diagnostic use for thyroid suppression testing.

The interference of biotin with some immunoassays, can be explained by the role that exogenous biotin plays in disrupting the streptavidin-biotin interaction which is the basis of these immunoassays and hence leading to falsely decreased or falsely increased test results, depending on the assay format.

Thyroid function tests evaluating the hypothalamic-pituitary-thyroid axis are conducted using immunoassays. Thyrotropin, free thyroxine and free triiodothyronine can be measured with sandwich or competitive assays. In a sandwich assay, the concentration of the substance being measured is directly proportional to the signal. In this case, extra biotin lowers the signal, causing falsely low values. In competitive immunoassays, the serum concentration of the particle measured is inversely proportional to the signal intensity, thus extra biotin levels cause falsely high values.

Given the increasingly common use of biotin supplements in high dosage and the prevalence of hypothyroidism with dependence on periodic measurement of thyroid function tests for adjustment of T4 dosage, there is potential for clinical mismanagement of these patients based on misleading test results.

In addition to this HCP communication, the product information (SmPC and package leaflet) of levothyroxine containing medicinal products will also be updated to reflect the risk of biotin interference with thyroid immunoassays.

Reporting of adverse reactions

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme.

Please report:

- all suspected ADRs that are serious or result in harm. Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle ▼

You can report via:

- the Yellow Card website
- 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.