

PLEASE READ

**IMPORTANT MEDICINE
SAFETY INFORMATION**

APPROVED
BY THE



Direct Healthcare Professional Communication (DHPC)

Date: 20-Jan-2023

Levothyroxine containing products: Biotin interference with laboratory tests.

Dear Healthcare Professional,

The marketing authorisation holders of levothyroxine, Amdipharm Limited and TEVA Pharmaceuticals in agreement with the European Medicines Agency and the Health Products Regulatory Authority (HPRA), 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.

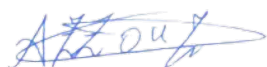
Call for reporting

Healthcare professionals are asked to report any suspected adverse reactions associated with these products in accordance with the national spontaneous reporting systems via HPRA Pharmacovigilance, website: www.hpra.ie

Company contact point

This information is being provided jointly by the Marketing Authorisation Holders (MAHs) listed in Table 1 below. Suspected adverse reactions should also be reported to the relevant MAHs.

Yours sincerely,



Nowel Redder

Associate Director Pharmacovigilance and Medical Affairs – EU QPPV

Amdipharm Limited, Ireland

And on behalf of:

Makarand Bagul

Dr. Makarand Bagul

Cluster Medical and Technical Senior Director – UK & IE

TEVA Pharmaceuticals Ireland

Table 1: Contact details for the Marketing Authorisation Holders for reporting adverse drug reactions

Marketing Authorisation Holder	Medicinal Product Full Name	Marketing Authorisation Number	Email contact	Phone
Amdipharm Limited, Ireland	Eltroxin 50 microgram Tablets	PA1142/028/001	medicalinformation@advanzpharma.com	+353 1800 851 119
	Eltroxin 100 microgram Tablets	PA1142/028/002		
	Eltroxin 25 microgram Tablets	PA1142/029/001		
	Levothyroxine 25 micrograms per 5 ml oral solution	PA1142/029/002		
	Levothyroxine 50 micrograms per 5 ml oral solution	PA1142/029/003		
	Levothyroxine 100 micrograms per 5 ml oral solution	PA1142/029/004		
TEVA Pharmaceuticals Ireland	Levothyroxine Teva 25 microgram Tablets	PA 0749/143/001	medinfo@tevauk.com	+44 (0) 207 540 7117
	Levothyroxine Teva 50 microgram Tablets	PA 0749/143/002		
	Levothyroxine Teva 100 microgram Tablets	PA 0749/143/003		