

## Levothyroxine: Biotin may interfere with thyroid immunoassays that are based on a biotin/streptavidin interaction

14.12.2022 | Circular Number P15/2022

### Information on levothyroxine, biotin and biotin containing medicines

- Levothyroxine is a synthetic thyroid hormone that is converted to triiodothyronine (T3) in peripheral organs and like the endogenous hormone, exerts specific effects at the T3 receptors.
- Levothyroxine is authorised in adults and children for the treatment of a number of conditions associated with hypothyroidism.
- Thyroid function tests look at levels of thyroid-stimulating hormone (TSH) and thyroxine (T4) in the blood and are used to check thyroid function and monitor patients on levothyroxine therapy.
- Biotin is a water-soluble B vitamin (B7) which is naturally present in some foods.
- Biotin may also be present at high dosages in food supplements and in biotin containing medicinal products.

The following biotin containing products are authorised via various national licensing procedures.

Active Ingredients	Product Name	Pharmaceutical Form	Classification	Authorisation Number	MAH/license holder
Alpha-Tocopherol, Inositol, <b>Biotin</b> , Folic Acid Thiamine Hydrochloride, Riboflavin, Pyridoxine Hydrochloride, Nicotinamide, Calcium pantothenate, Ascorbic Acid, Acetomenaphthone	Ketovite Tablets	Tablet	POM	AA565/02702	Central Procurement & Supplies Unit
<b>Biotin</b>	Biotin-ratiopharm 5mg Tablets	Tablet	POM	AA565/50501	Central Procurement & Supplies Unit
Folic acid, Ascorbic acid, <b>Biotin</b> , Calcium, Colecalciferol, Copper, Cyanocobalamin, D1-alfa-tocopherol, Panax ginseng extract, Nicotinamide, Thiamine mononitrate, Zinc, Iron, Magnesium, Manganese, Selenium, Lecithin, Pyridoxine hydrochloride, Retinol, Riboflavin	Pharmaton Capsules	Soft Capsule	POM	MA186/00301	Aldox Ltd.
Thiamine mononitrate, Nicotinamide, Sodium pantothenate, <b>Biotin</b> ,	Soluvit Powder for Solution	Powder for solution	POM	AA1123/02401	Fresenius Kabi Italia S.r.l

Cyanocobalamin, Riboflavin, Sodium phosphate, Pyridoxine hydrochloride, Sodium ascorbate, Folic acid	for Infusion	for infusion			
Panax ginseng extract, Vitamin A, Colecalciferol, DL-?-Tocopherol, Thiamine mononitrate, Riboflavin, Pyridoxine hydrochloride, Cyanocobalamin, <b>Biotin</b> , Nicotinamide, Ascorbic acid, Folic acid, Copper sulphate monohydrate, Sodium selenite, Magnesium sulfate, Iron, Zinc sulfate, Dibasic potassium phosphate anhydrous, Lecithin	Pharmaton Vitality Capsule	Soft Capsule	OTC	AA908/16201	NeoFarma Pharmaceuticals Limited

### Information from the EMA about the safety concern

- The Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) has endorsed the Pharmacovigilance Risk Assessment Committee (PRAC) recommendations on the periodic safety update report single assessment (PSUSA) for levothyroxine. The following Key messages concerning biotin interference with laboratory tests for levothyroxine are communicated: 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.
- During the PSUSA assessment the PRAC considered the available data on biotin interference with thyroid function tests from spontaneous reports and literature. The majority of the described cases have compatible chronology without confounding factors, laboratory test results returned to normal following withdrawal of biotin or use of a different assay method. In view of the available data, a causal association of laboratory interference with biotin was identified.
- 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 significant potential for clinical mismanagement of these patients based on misleading test results.
- Determination of biotin intake would be particularly important in situations requiring more exact titration of levothyroxine dosage, such as in pregnant women, in children, in the elderly, and in patients being monitored for residual or recurrent thyroid cancer.

## **More about the procedure**

This safety issue was described in the context of periodic safety update report single assessment (PSUSA) for levothyroxine. The PRAC recommendation has been forwarded to the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh). The CMDh has endorsed the PRAC’s position and the product information of levothyroxine containing products should be amended accordingly through a submission of a variation by the Marketing Authorisation Holder concerned.

## **Information to Healthcare Professionals**

- Biotin may interfere with thyroid immunoassays that are based on a biotin/streptavidin interaction, leading to either falsely decreased or falsely increased test results. The risk of interference increases with higher doses of biotin.
- When interpreting results of laboratory tests, possible biotin interference has to be taken into consideration, especially if a lack of coherence with the clinical presentation is observed.
- For patients taking biotin-containing products, laboratory personnel should be informed when a thyroid function test is requested. Alternative tests not susceptible to biotin interference should be used, if available.

## **Information to patients**

- If you are about to undergo laboratory testing for monitoring your thyroid hormone levels, you must inform your doctor and/or the laboratory personnel that you are taking or have recently taken biotin (also known as vitamin B, vitamin B7 or vitamin B8).
- Biotin may affect results of your laboratory tests. Depending on the test, the results may be falsely high or falsely low due to biotin. Your doctor may ask you to stop taking biotin before performing laboratory tests.
- You should also be aware that other products that you may take, such as multivitamins or supplements for hair, skin, and nails could also contain biotin. This could affect the results of laboratory tests. Please inform your doctor and/or the laboratory personnel, if you are taking such products

## **Reporting Adverse Drug Reactions**

Healthcare professionals and patients are encouraged to maintain vigilance with biotin, and levothyroxine, containing 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**

**Medicines Authority**

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

**Feedback Form**

The 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 Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this form (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.

Postage will be paid  
by the Licensee

No postage stamp  
necessary if posted  
in Malta and Gozo

**BUSINESS REPLY SERVICE**

Licence no. 656

Pharmacovigilance Section  
Post-Licensing Directorate  
Medicines Authority  
Sir Temi Żammit Buildings  
Malta Life Sciences Park  
San Ġwann SĠN 3000