Is there an interaction between orlistat and levothyroxine?

Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals

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Background

Orlistat is an anti-obesity drug available on prescription as a 120mg capsule (Xenical®), or over-the-counter as a 60mg capsule (Alli®). The National Institute for Health and Clinical Excellence (NICE) recommends that orlistat is used in adults with a body mass index (BMI) of 30 or with a BMI of 28 or more along with associated risk factors and is initiated after dietary and lifestyle changes have been attempted but a target weight has not been reached by these measures alone (1). The Medicines and Healthcare Regulatory Agency (MHRA) issued a Drug Safety Update in February 2010 which raised awareness of a possible interaction between levothyroxine and orlistat (2). This Q&A details the current evidence behind this interaction and how to manage patients.

Answer

Orlistat acts by inhibiting lipases in the stomach and small intestine, which in turn means that triglycerides in dietary fat are not broken down into fatty acids. This reduces absorption of fat into the body. Undigested fat is then excreted in the faeces. Orlistat is minimally absorbed systemically and appears to be mainly metabolised in the gastro-intestinal tract. The majority of the drug is excreted unchanged in the faeces (3). Side effects of orlistat are mainly mild to moderate gastro-intestinal effects but rarely serious liver disorders have been reported (2).

Evidence of Interaction

Only two case reports of an interaction between levothyroxine and orlistat have been reported in the literature. One details a 46 year old woman who was taking 250 micrograms of levothyroxine following total thyroidectomy due to papillary carcinoma of the thyroid. Two weeks after commencing orlistat therapy, she suffered symptoms of hypothyroidism which improved following withdrawal of orlistat and an increase of levothyroxine to 300 micrograms (4). The other case report describes a 43 year old woman who experienced a gradual change in TSH levels, requiring an increase in dosage of levothyroxine. Following discontinuation of orlistat, her TSH levels normalised with a resulting slow decrease in dosage (5).

Mechanism of interaction

Due to its rarity, the cause of this interaction is as yet unknown, but it is postulated that orlistat may bind to levothyroxine, limiting its absorption into the gastro-intestinal tract (3). To date, no common metabolism pathways or plasma protein binding sites have been discovered for the two drugs (5). Levothyroxine absorption is decreased by steatorrhoea and malabsorption, which may occur due to the action of orlistat (6). Another mechanism may be a reduced absorption of iodine salts. Iodine salts are converted to iodide in the gastro-intestinal tract, which in turn is oxidised and incorporated into levothyroxine (T4) and tri-iodothyronine (T3) (7). Hence reduction in iodine absorption may lead to hypothyroidism.

Management of Interaction

The summary of product characteristics (SPC) for Alli® was amended in 2009 to include a warning regarding hypothyroidism and to clarify that patients wishing to take orlistat should speak to their GP prior to treatment (8). As evidence of the clinical importance of this interaction is lacking however, the possibility of an interaction should not stop co-administration of these drugs. The administration of levothyroxine and orlistat should be separated by 4 hours, and increased monitoring of the patient’s thyroid hormone levels may be prudent (9, 10).
Summary

♦ A potential interaction exists between levothyroxine and orlistat.
♦ This may be due to reduced absorption of levothyroxine, or iodine, or both.
♦ This interaction is not a contra-indication to use of orlistat along with levothyroxine.
♦ Patients should be advised to speak to their GP prior to purchasing orlistat over-the-counter if they are also taking levothyroxine.
♦ Orlistat and levothyroxine should be administered at least 4 hours apart.
♦ The patient's thyroid hormone levels should be monitored.

Limitations
Documented evidence of this interaction is lacking, so the available evidence is difficult to interpret.

Quality Assurance

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Search strategy
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NICE website
MHRA website
Electronic Medicines Compendium
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