ANNEX I

LIST OF THE INVENTED NAME, PHARMACEUTICAL FORM, STRENGTH OF THE MEDICINAL PRODUCT, ROUTE OF ADMINISTRATION AND MARKETING AUTHORISATION HOLDER IN THE MEMBER STATES (EEA)

IODOCASEIN/THIAMINE CONTAINING MEDICINAL PRODUCTS WITH MARKETING AUTHORISATION IN THE EUROPEAN UNION

Member State	Marketing Authorisation Holder	Invented Name	Strength	Pharmaceutical Form	Route of administration
Italy	TEOFARMA SRL Via Fratelli Cervi, 8 Valle Salimbene 27010 PAVIA Italy	ANTIADIPOSO	125 mg + 12,33 mg	Coated tablet	Oral use

ANNEX II

SCIENTIFIC CONCLUSIONS AND GROUNDS FOR THE REVOCATION OF THE MARKETING AUTHORISATION

SCIENTIFIC CONCLUSIONS

OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF MEDICINAL PRODUCT(S) CONTAINING IODOCASEIN/THIAMINE (see Annex I)

Iodocasein 125mg (7.6% of iodine) and thiamine as nitrate 12.33 mg are the active substances for Antiadiposo, approved since 1955 in Italy for the treatment of obesity resulting from metabolic disorders. The therapeutic effect of Antiadiposo is mainly due to iodocasein, which increases the amount of available iodine, stimulating the thyroid gland and consequently activating the metabolic processes.

On 16 September 2009, the Italian Competent Authority (AIFA) issued a Rapid Alert informing the Members States, the EMEA and the European Commission (EC) in accordance with Article 107 of Directive 2001/83/EC, as amended, of the suspension of the Marketing Authorisation of iodocasein/thiamine containing medicinal product (Antiadiposo) in its Member State, due to serious cases of hyperthyroidism and thyrotoxicosis.

The CHMP discussed the matter at its September 2009 plenary meeting and the procedure in accordance with Article 107(2) of Directive 2001/83/EC, as amended was started.

Safety

Cases of hyperthyroidism and thyrotoxicosis, 12 and 3, respectively were reported in subjects being treated with iodocasein/thiamine. These clinical conditions translate the overproduction and consequent excess of circulating free thyroid hormones with effects in every type of tissue. This over stimulation of the metabolism is also frequently accompanied by tachycardia, palpitations and anxiety. All reported cases were related with iodocasein/thiamine and 6 cases considered serious.

The majority of the cases occurred at a dose of two tablets *per* day treatment which is the recommended daily dose. However, this daily dose represents an iodine dose intake which is 120 times higher than the recommended daily dose.

There have been publications on the iodine–induced hyperthyroidism which may occur in patients with iodine-deficiency and thyroid dysfunction but also in patients with no evidence of underlying thyroid disease.

The product information lists hyperthyroidism as a contra-indication and advises on the need for a regular control of the thyroid function during treatment with recommendation for discontinuation of the treatment in case of abnormal tests results of thyroid function, with symptoms of hyperthyroidism, tachycardia and arrhythmia.

However, this measure is not sufficient to address the risks for hyperthyroidism and thyrotoxicosis associated with the iodocasein/thiamine treatment as above described.

Benefits

Antiadiposo has been used for the treatment of obesity. However, the benefits of thyroid hormone therapy in inducing weight loss in obese subjects during caloric deprivation or on morbidity and mortality in patients with non thyroidal illnesses are not clear from published data.

Benefit/risk

Antiadiposo (iodocasein 125 mg/thiamine 12.33 mg), approved since 1955 in Italy for the treatment of obesity acts by increasing the amount of available iodine thus stimulating the thyroid gland and consequent metabolic processes. The amount of iodine released *per* each tablet (i.e. 9.4 mg) is noted to be 60 times higher than the daily recommended iodine dose of 150 mcg.

Serious cases of hyperthyroidism and thyrotoxicosis, related with iodocasein/thiamine treatment have been reported. The majority of the cases occurred at a dose of two tablets *per* day which is the recommended daily dose.

Available data are insufficient to enable the demonstration of the benefits of thyroid hormone therapy in inducing weight loss in obese subjects during caloric deprivation or on morbidity and mortality in patients with non thyroidal illnesses. Whereas, there are data supporting that thyroid hormone therapy, even at physiological doses, may induce subclinical hyperthyroidism in obese subjects during caloric deprivation and in patients with non-thyroidal illnesses resulting in detrimental effects.

Taking all the above elements in consideration and the fact that there are other therapeutic alternatives available for the treatment of obesity, the CHMP concluded that the benefit/risk balance for iodocasein/thiamine is not considered favourable and recommended the revocation of the Marketing Authorisation for the medicinal product referred to in Annex I.

GROUNDS FOR THE REVOCATION OF THE MARKETING AUTHORISATIONS

Whereas,

- The Committee considered the procedure under Article 107 of Directive 2001/83/EC, as amended, for medicinal products containing iodocasein/thiamine.
- The Committee concluded, after having reviewed the available data, that iodocasein/thiamine is associated with serious cases of hyperthyroidism and thyrotoxicosis.
- The Committee considered that clear evidence on the benefits of iodocasein/thiamine in the treatment of obesity is lacking.
- The Committee noted that iodocasein/thiamine is approved for a condition for which alternative treatments are available.
- The Committee, in light of the above findings, concluded that the benefit/risk balance of iodocasein/thiamine containing medicinal products is not favourable.

Following the provisions under Article 107(2) of Directive 2001/83/EC, as amended, the Agency's Committee for Medicinal Products for Human Use (CHMP) prepared an opinion on 22 October 2009 recommending the revocation of the Marketing Authorisation for iodocasein/thiamine containing medicinal product referred to in Annex I.