CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-121

PROPRIETARY NAME REVIEW(S)

MEMORANDUM	**Division of Medication Errors and Technical Support (DMETS)** **Office of Surveillance and Epidemiology** **WO22, Mail Stop 4447** **Center for Drug Evaluation and Research**

TO: Mary H. Parks, M.D.
Director, Division of Metabolism and Endocrinology Products (HFD-510)

THROUGH: Todd Bridges, R.Ph., Team Leader
Denise Toyer, Pharm.D., Deputy Director
Carol Holquist, R.Ph., Director
Division of Medication Errors and Technical Support, WO22, Mail Stop 4447

FROM: Diane C. Smith, Pharm.D., Safety Evaluator
Division of Medication Errors and Technical Support, WO22, Mail Stop 4447

DATE: June 5, 2007

SUBJECT: DMETS Label and Labeling Review
Drug: Tirosint (Levothyroxine Sodium Capsules) 13 mcg
NDA#: 22-121
Sponsor: IBSA Biochimique SA

PROJECT #: 2007-1224

This memorandum is in response to a May 29, 2007, request from the Division of Metabolism and Endocrinology Products (HFD-510) for a review of the revised container label and carton labeling of Tirosint 13 mcg. The label and labeling revisions were made in response to DMETS' OSE Review #2007-677, dated April 12, 2007.

DMETS acknowledges that the sponsor has addressed most of our recommendations. However, upon review of the sponsor's response and revised labels and labeling, we have the following comments:

A. GENERAL COMMENT

In response to our request for information on the manufacturer's point of contact in the United States, the sponsor states that a point of contact has not been identified. The sponsor indicates that once a United States distributor has been identified it will be added to the labeling. However, healthcare providers and patients should have a point of contact in the United States in order to report medication errors and adverse events. Additionally, if healthcare providers need further information on Tirosint there is no way for them to obtain this information from a company representative. The address listed in the labeling is for a Swedish contact and the Internet site is not in English. Thus, DMETS believes that patient safety may be jeopardized if this product is distributed without a contact in the United States listed in the labels and labeling before approval.

B. INSERT LABELING

DMETS recommends implementation of the label and labeling revisions outlined above in order to minimize potential user error. Please copy DMETS on any correspondence to the sponsor pertaining to this issue. DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, OSE Project Manager, at 301-796-0080.

Appears This Way
On Original

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Diane Smith
6/13/2007 05:00:00 PM
CSO

Todd Bridges
6/13/2007 05:03:38 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
6/14/2007 07:27:35 AM
DRUG SAFETY OFFICE REVIEWER

MEMORANDUM	Division of Medication Errors and Technical Support Office of Surveillance and Epidemiology HFD-420; White Oak Bldg. 22, Mail Stop 4447 Center for Drug Evaluation and Research

TO: Mary Parks, M.D.
Director, Division of Metabolism and Endocrinology Products, HFD-510

THROUGH: Linda Y. Kim-Jung, Pharm.D., Team Leader
Denise Toyer, Pharm.D., Deputy Director
Carol Holquist, R.Ph., Director
Division of Medication Errors and Technical Support, HFD-420

FROM: Todd Bridges, R.Ph., Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

DATE: April 5, 2007

SUBJECT: DMETS Label and Labeling Review
Drug: Tirosint
(Levothyroxine Sodium Capsules) 13 mcg
NDA #: 22-121
Sponsor: Institut Biochimique SA

SE REVIEW #: 2007-677

This memorandum is in response to a March 22, 2007, request from the Division of Metabolism and Endocrinology Products (HFD-510) for a review of the container label and carton and insert labeling for Tirosint Capsules 13 mcg.

Tirosint was approved on October 13, 2006, for the following strengths: 25 mcg, 50 mcg, 75 mcg, 100 mcg, 125 mcg, and 150 mcg. However, the 12.5 mcg strength was not approved because of the potential for the 12.5 mcg and 125 mcg product strengths to be confused by pharmacists and patients and the clinical consequences of such a medication error. Thus, Tirosint 12.5 mcg was administratively unbundled from NDA #21-924 and assigned NDA #22-121. Subsequently, NDA #22-121 was re-submitted for Tirosint 13 mcg.

Since Tirosint is currently marketed, DMETS conducted a search of the FDA *Adverse Event Reporting System* (AERS) for all post-marketing safety reports of medication errors associated with Tirosint. AERS was searched using the tradename "Tirosint" with MedDRA High Level Terms "Medication Errors Due to Accidental Exposures", "Overdoses", "Maladministrations", "Medication Monitoring Errors", and "Medication Errors NEC". This search did not retrieve any cases of postmarketing confusion with the nomenclature, labels, or labeling of Tirosint.

Upon review of the label and labeling of Tirosint 13 mcg, DMETS has identified the following areas of improvement, in the interest of minimizing user error and maximizing patient safety.

A. GENERAL COMMENTS

1. Ensure that the established name is at least ½ the size of the proprietary name and that it appears prominently in accordance with 21 CFR 201.10(g)(2).

2. As currently presented, patients may misinterpret the statement of product strength as the total amount of Tirosint contained in an entire blister card. DMETS has received reports of medication errors of this type which involved products in which the strength was expressed in the same manner as proposed for this product. Therefore, we request that you revise the statement of strength to read "13 mcg per capsule" or "13 mcg/capsule" in order to prevent patients from ingesting the wrong dose (e.g., the entire contents of the blister card).

3. The distributor named is located in Switzerland (CH). Provide information on the manufacturer's point of contact in the United States.

4. As currently presented, the statement of product strength "13 mcg" (white text on the lime green background) is difficult to read. To help improve readability, the text font color utilized should maximize the contrast between the text and the background. However, ensure that the color utilized does not overlap or look-similar to any color used to identify other Tirosint strengths.

B. BLISTER LABELS

1. See GENERAL COMMENTS A1 through A3.

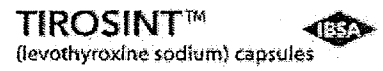
2. The label submitted indicates that the text will be printed on aluminum foil. The lime green color proposed to identify the 13 mcg product strength may be difficult to discern on the foil background. To help improve readability, the color used should maximize the contrast between the text and the foil background.

3. In the current presentation, it is possible for individual blisters to become separated from the blister card. This scenario is most likely to occur in hospitals where capsules are dispensed as unit dose but it can also occur on an outpatient basis as well. For example, patients may cut individual blisters from the blister card for convenience and storage. Such labeling with other products has resulted in medication errors in which the blister card was cut up into unidentifiable blisters. Therefore, please ensure that each blister cell is labeled with the proprietary name, strength, lot number, expiration date, and distributor so practitioners and patients will always have this information readily available.

C. CARTON LABELING

1. See GENERAL COMMENTS A1 through A4.

2.



3.

4. statement should be revised to read "Usual Dosage: See package insert for dosage information." We refer you to 21 CFR 201.55 for guidance.

5. Revise the presentation of the net quantity to read "8 unit dose blisters x 7 capsules each".

6. Revise ' to read "Lot:" and "Exp:", respectively.

D. INSERT LABELING

1.

2. HOW SUPPLIED

See GENERAL COMMENT A3.

Appears This Way
On Original

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Todd Bridges
4/12/2007 04:02:49 PM
DRUG SAFETY OFFICE REVIEWER

Linda Kim-Jung
4/12/2007 04:08:28 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
4/12/2007 04:56:50 PM
DRUG SAFETY OFFICE REVIEWER

MEMORANDUM	**Division of Medication Errors and Technical Support** **Office of Surveillance and Epidemiology** **(HFD-420; White Oak Bldg. 22, Mail Stop 4447)** **Center for Drug Evaluation and Research**

TO: Mary Parks, M.D.
Director, Division of Metabolism and Endocrinology Products, HFD-510

THROUGH: Linda Y. Kim-Jung, Pharm.D., Team Leader
Denise Toyer, Pharm.D., Deputy Director
Carol Holquist, R.Ph., Director
Division of Medication Errors and Technical Support, HFD-420

FROM: Todd Bridges, R.Ph., Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

DATE: November 14, 2006

SUBJECT: DMETS Labeling Review
Drug: Tirosint
(Levothyroxine Sodium Capsules) 12.5 mcg
NDA #: 22-121
Sponsor: Institut Biochimique SA

OSE REVIEW #: 2006-766

This memorandum is in response to an October 18, 2006 request from the Division of Metabolism and Endocrinology Products (HFD-510) for assessment of the container label and carton labeling of Tirosint 12.5 mcg.

In OSE review 06-0015 (dated October 2, 2006), DMETS did not recommend approval of this strength, 12.5 mcg due to potential for confusion with the 125 mcg product strength. DMETS recommended that in lieu of the 12.5 mcg strength, the sponsor market a non-overlapping number strength such as 12 mcg or 13 mcg. DMETS also recommended that the sponsor ensure that any alternate strength selected does not overlap numerically with other available strengths of Tirosint (e.g., 10 mcg strength would overlap with the 100 mcg strength). Because of the potential for a ten-fold over or under-dose, DMETS does not believe this product strength should coexist in the marketplace with the 125 mcg strength. The 12.5 mcg is not a "must have" strength and approving this strength would introduce unnecessary risk of patient harm if the 12.5 mcg strength was confused for the 125 mcg and vice versa.

Because of the safety concerns, Tirosint was approved on October 13, 2006 without the 12.5 mcg strength. Tirosint 12.5 mcg was administratively unbundled from NDA #21-924 and assigned NDA #22-121.

DMETS continues to recommend that in lieu of the 12.5 mcg strength, a non-overlapping strength such as 12 mcg or 13 mcg be considered. Additionally, the sponsor should ensure that any alternate strength selected does not overlap with other available strengths of Tirosint (e.g., a 10.0 mcg strength would overlap with the 100 mcg strength).

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Diane Smith, Project Manager, at 301-796-0538.

Appears This Way
On Original

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Linda Kim-Jung
11/27/2006 01:33:47 PM
DRUG SAFETY OFFICE REVIEWER
Also signing for Todd Bridges 11/27/06.

Denise Toyer
11/27/2006 01:59:32 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
11/27/2006 02:21:53 PM
DRUG SAFETY OFFICE REVIEWER