CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-924

PROPRIETARY NAME REVIEW(S)

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

PROPRIETARY NAME, LABEL, AND LABELING REVIEW

DATE OF REVIEW: January 31, 2006

NDA#: 21-924

NAME OF DRUG: **Tirosint ™**
(Levothyroxine Sodium Capsules)
12.5 mcg, 25 mcg, 50 mcg, 75 mcg, 100 mcg,
125 mcg, and 150 mcg

NDA HOLDER: Institut Biochimique SA

I. INTRODUCTION:

This consult was written in response to a request from the Division of Metabolism and Endocrinology Products (HFD-510), for assessment of the proprietary name, Tirosint™, regarding potential name confusion with other proprietary or established drug names. The proposed container labels, carton and insert labeling were submitted for review and comment.

PRODUCT INFORMATION

Each Tirosint™ capsule contains synthetic levothyroxine (T4) sodium. Levothyroxine is the principal hormone secreted by the thyroid gland. The primary effect of thyroid hormones is to increase the metabolic rate of most body tissues. Tirosint™ is indicated as replacement or supplemental therapy in congenital or acquired hypothyroidism, for the treatment or prevention of various types of euthyroid goiters, and as an adjunct to surgery and radioiodine therapy in the management of thyroid cancer. The usual dosage range is 12.5 mcg to 300 mcg once daily and is dependent upon a variety of factors including the patient's age, body weight, cardiovascular status, concomitant medical conditions, concomitant medications, and the specific nature of the condition being treated. Tirosint™ capsules are available in seven strengths: 12.5 mcg, 25 mcg, 50 mcg, 75 mcg, 100 mcg, 125 mcg, and 150 mcg.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1,2] as well as several FDA databases[3,4] for existing drug names which sound-alike or look-alike to Tirosint to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted[5]. The SAEGIS[6] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Tirosint. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proposed proprietary name, Tirosint, acceptable from a promotional perspective.

2. The Expert Panel identified one proprietary name that was thought to have the potential for confusion with Tirosint. This product is listed in Table 1 (see page 4), along with the dosage form available and usual dosage.

---

[1] MICROMEDEX Integrated Index, 2006, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, Missouri.

[3] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-06, and the electronic online version of the FDA Orange Book.

[4] Phonetic and Orthographic Computer Analysis (POCA)

[5] www location http://www.uspto.gov/tmdb/index.html

[6] Data provided by Thomson & Thomson's SAEGIS™ Online service, available at www.thomson-thomson.com

III. COMMENTS TO THE SPONSOR:

DMETS does not recommend the use of the proprietary name, Tirosint. In reviewing the proprietary name Tirosint, the primary concern relating to look-alike confusion with Tirosint is Triostat. DMETS also has concerns with the potential for confusion between the 12.5 mcg and 125 mcg strengths.

A. Look-Alike Name Concerns

DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with the aforementioned name. However, negative findings are not predictive as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Tirosint.

In review of the name Tirosint, Triostat was found to look similar to Tirosint when scripted. Triostat is indicated for the treatment of myxedema coma/precoma, a rare, life-threatening clinical condition which is usually precipitated in the hypothyroid patient of long standing by intercurrent illness or drugs such as sedatives and anesthetics. Therapy for this condition includes correction of electrolyte disturbances, possible infection, or other intercurrent illness in addition to the simultaneous administration of intravenous liothyronine (T_3) and glucocorticosteroids. Triostat is supplied in 1 mL vials to be administered intravenously.

Triostat and Tirosint both begin and end with the same letter "t" and overlap with the same letters at the fourth, fifth ("os") and eight ("t") position of each name. Furthermore, the second and third letters of each name ("ri" vs. "ir") are also the same but are inverted. However, the letters "ta" of Triostat differ from the letters "in" of Tirosint which may help to distinguish this name pair (see below).

We recognize that there are different product characteristics such as dosage form (tablet vs. injection), route of administration (oral vs. intravenous), available strengths (12.5 mcg; 25 mcg, 50 mcg, 75 mcg, 100 mcg, 125 mcg, and 150 mcg vs. 10 mcg/mL), dosing frequency (once daily vs. individualized dosing at which at least four hours, but no more than twelve hours should be allowed between doses), and indication of use (hypothyroidism vs. myxedema coma/precoma).

However, despite the aforementioned differences there are some characteristics which when considered makes the products appear more similar. These include similar established names (Levothyroxine Sodium vs. Liothyronine Sodium), same unit of measure (mcg) and both products can have an overlapping dosing range from 10 mcg to 50 mcg. Because there is similarity with not only the proprietary name but also the established names, and the fact that the dosing and unit of measure are the same increases the risk of product confusion. Another concern is that the established name can be written on an order in lieu of the tradename. This is not an unlikely scenario as Levothyroxine Sodium is available in several different tradenames (e.g., Synthroid, Levoxyl, Levothroid, etc) and thus, the prescriber may not necessarily indicate the

3 Page(s) Withheld

✓ Trade Secret / Confidential

_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Proprietary Name Review- 1

Appendix A: DMETS prescription study results for Tirosint.

Inpatient	Voice	Outpatient
Tionint	Luosint	Ferosint
Tironint	Tarosin	Ferosint
Tironint	Tyra(o)sent	Fuosint
Tironist	Tyrafent	Fuosint
Tironist	Tyrocept	Jirosint
Tironsert	Tyrocid	Juosint
Tirosint	tyroscint	Liosint
Tirosint	tyrosent	Lirosint
Tirosint	Tyrosent	Lirosint
Tirosint	Tyrosid	Luosint
Tirosint	Tyrosin	Luosint
Tirosint	tyrosint	Luosint
Tirosint	Tyrosint	Luosint
Tirosint	Tyrosint	Lurosint
Tirosint		Tirosint
Tirosint		Tirosint
Tirosint		Triosint
Tirosint		Triosint
Tirosint		Triosint
Tirosint		Tuosint
Tirosint		Turosint
Tirovist		Urosint
Tisosnet		
Tixonint		

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
10/2/2006 02:40:19 PM
DRUG SAFETY OFFICE REVIEWER

Linda Kim-Jung
10/2/2006 02:43:11 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
10/2/2006 03:57:08 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
10/2/2006 04:07:18 PM
DRUG SAFETY OFFICE REVIEWER