DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Clarence E. Jones, Ph.D.,
Institut Biochimique SA (IBSA) U.S. Agent
Institut Biochimique SA
4249 Via Encanto
Thousand Oaks, CA 91320

RE: NDA #021924
TIROSINT (levothyroxine sodium) capsules, for oral use
MA #42

Dear Dr. Jones:

This letter notifies Institut Biochimique SA (IBSA) and, by copy, Akrimax Pharmaceuticals, LLC (Akrimax), U.S. agent for TIROSINT (levothyroxine sodium) capsules for oral use (Tirosint), that as part of its monitoring and surveillance program, the Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed IBSA's Facebook webpage for Tirosint.[1] The Facebook webpage is false or misleading because it makes representations about the efficacy of Tirosint, but fails to communicate any risk information associated with its use and it omits material facts. Thus, the Facebook webpage misbrands Tirosint within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act), and makes its distribution violative. 21 U.S.C 352(a), (n); 321(n); 331(a). *See* 21 CFR 202.1(e)(5).

Background

Below are the indication (in pertinent part) and summary of the most serious and most common risks associated with the use of Tirosint.[2] According to the INDICATIONS AND USAGE section of the FDA-approved product labeling (PI):

> TIROSINT is indicated as a replacement or supplemental therapy in congenital or acquired hypothyroidism of any etiology, except transient hypothyroidism during the recovery phase of subacute thyroiditis. Specific indications include: primary (thyroidal), secondary (pituitary), and tertiary (hypothalamic) hypothyroidism. Primary hypothyroidism may result from functional deficiency, primary atrophy, partial or total congenital absence of the thyroid gland, or from the effects of surgery, radiation, or drugs, with or without the presence of goiter.

[1] Tirosint Facebook webpage, at https://www.facebook.com/pages/Tirosint-Levothyroxine-Sodium-Capsules/123553291015984 (Last accessed February 24, 2014)
[2] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece(s) cited in this letter.

Tirosint is associated with a number of serious risks. The PI for Tirosint includes a Boxed Warning indicating that Tirosint should not be used for the treatment of obesity or for weight loss. Tirosint is contraindicated in patients who may be unable to swallow a capsule including young children, in patients with acute myocardial infarction, and in patients with uncorrected adrenal insufficiency. The PI for Tirosint also includes Warnings and Precautions regarding the importance of proper dose titration to prevent hyperthyroidism or incomplete treatment of hypothyroidism, risk of cardiac adverse reactions in the elderly and in patients with underlying cardiovascular disease, patients with nontoxic diffuse goiter or nodular thyroid disease, patients with concomitant adrenal insufficiency, and thyroid hormone over-replacement associated with decreased bone mineral density.

The common adverse reactions are primarily those of hyperthyroidism due to therapeutic overdosage including: irregular heartbeat, chest pain, shortness of breath, leg cramps, headache, nervousness, irritability, insomnia, tremors, muscle weakness, change in appetite, weight change, diarrhea, heat intolerance, changes in menstrual periods, and skin rash.

Omission of Risk Information

Promotional materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials. The Facebook webpage includes the following presentation (bolded emphasis original):

> "**Tirosint® (Levothyroxine Sodium) Capsules**
>
> . . .
>
> If you have just been diagnosed with hypothyroidism or are having difficulty controlling your levothyroxine blood levels, talk to your doctor about prescription Tirosint, a unique liquid gel cap form of levothyroxine."

The Facebook webpage is misleading because it makes representations about the efficacy of Tirosint, but fails to communicate **any** of the risks associated with its use. This omission of risk information is particularly concerning considering that the Tirosint PI includes a Boxed Warning. By omitting the most serious and frequently occurring risks associated with Tirosint, the Facebook webpage misleadingly suggests that Tirosint is safer than has been demonstrated.

Omission of Material Facts

The Facebook webpage fails to provide material information regarding Tirosint's FDA-approved indication. While the Facebook webpage makes suggestions regarding the use of Tirosint in patients with hypothyroidism, it fails to convey that Tirosint is not indicated for transient hypothyroidism during the recovery phase of subacute thyroiditis. Specifically, the INDICATIONS AND USAGE section of the PI states the following (bolded emphasis added):

Tirosint is indicated as a replacement or supplemental therapy in congenital or acquired hypothyroidism of any etiology, **except transient hypothyroidism during the recovery phase of subacute thyroiditis.**

Conclusion and Requested Action

For the reasons discussed above, the Facebook webpage misbrands Tirosint within the meaning of the FD&C Act, and makes its distribution violative. 21 U.S.C 352(a), (n); 321(n); 331(a). *See* 21 CFR 202.1(e)(5).

OPDP requests that IBSA immediately cease violating the FD&C Act, as discussed above. Please submit a written response to this letter on or before March 10, 2013, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for Tirosint that contain presentations such as those described above, and explaining your plan for discontinuing use of such materials.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266** or by facsimile at (301) 847-8444. To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. Please refer to MA #42 in addition to the NDA number in all future correspondence relating to this particular matter. All correspondence should include a subject line that clearly identifies the submission as a Response to an Untitled Letter. OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your distribution of Tirosint complies with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Kendra Y. Jones
Regulatory Review Officer
Office of Prescription Drug Promotion

{See appended electronic signature page}

Adora Ndu, Pharm.D.
Acting Team Leader
Office of Prescription Drug Promotion

cc: Keith S. Rotenberg, Ph.D.
Corporate Vice President & Chief Scientific Officer
Akrimax Pharmaceuticals, LLC
11 Commerce Drive, 1st Floor
Cranford, NJ 07016

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/s/

KENDRA Y JONES
02/24/2014

ADORA NDU
02/24/2014