DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Sanjiv Sharma, Vice President, Commercial Operations
Duchesnay, Inc.
919 Conestoga Road
Building One, Suite 203
Rosemont, PA 19010

RE: NDA # 021876
DICLEGIS (doxylamine succinate and pyridoxine hydrochloride) delayed-release tablets, for oral use
MA # 3

Dear Mr. Sharma:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a letter (2013-0032-01) announcing the approval of DICLEGIS (doxylamine succinate and pyridoxine hydrochloride) delayed-release tablets, for oral use (DICLEGIS) submitted by Duchesnay, Inc. (Duchesnay) under cover of Form FDA 2253. The letter is false or misleading in that it presents efficacy claims for DICLEGIS, but fails to communicate any risk information associated with its use and it omits material facts. Thus, the letter misbrands the drug in violation of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), 21 U.S.C. 352(a) & 321(n). *Cf.* 21 CFR 202.1 (e)(5). In addition, Duchesnay did not comply with 21 CFR 201.10(g)(1) and it appears that Duchesnay also did not comply with 21 CFR 201.100(d).

Background

Below are the indication and summary of the most serious and most common risks associated with the use of DICLEGIS.[1]

According to its FDA-approved product labeling (PI) (emphasis in original):

> DICLEGIS is indicated for the treatment of nausea and vomiting of pregnancy in women who do not respond to conservative management.
>
> **Limitations of Use**
>
> DICLEGIS has not been studied in women with hyperemesis gravidarum.

[1] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece cited in this letter.

DICLEGIS is contraindicated in women with known hypersensitivity to doxylamine succinate, other ethanolamine derivative antihistamines, pyridoxine hydrochloride or any inactive ingredient in the formulation, as well as in women who are taking monoamine oxidase inhibitors (MAOIs). The PI for DICLEGIS includes Warnings and Precautions regarding activities requiring mental alertness and concomitant medical conditions. In addition, the most common adverse reaction reported with DICLEGIS was somnolence.

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 letter is misleading in that it presents various efficacy claims for DICLEGIS, but fails to communicate any risk information. For example, the letter includes claims such as:

- "Today I am pleased to inform you that the U.S. Food and Drug Administration has approved Diclegis® indicated for the treatment of nausea and vomiting of pregnancy (NVP) in women who do not respond to conservative management."
- "Millions of pregnant women could benefit from an approved NVP treatment and Diclegis represents a much needed FDA-approved treatment option."

The letter, however, entirely omits **all** risk information, including the contraindications, warnings and precautions, and the most frequently reported adverse event for DICLEGIS. By omitting the most serious and frequently occurring risks associated with the drug, the letter misleadingly suggests that DICLEGIS is safer than has been demonstrated.

Omission of Material Fact

The letter fails to provide material information regarding DICLEGIS' full approved indication, including important limitations of use. While we acknowledge that the letter communicates that DICLEGIS is indicated for the treatment of nausea and vomiting of pregnancy (NVP) in women who do not respond to conservative management, it fails to convey that DICLEGIS has not been studied in women with hyperemesis gravidarum. Specifically, the Indications and Usage section of the PI states the following (emphasis in original):

> **Limitations of Use**
>
> DICLEGIS has not been studied in women with hyperemesis gravidarum.

Inadequate Presentation of Established Name

The letter fails to present the established name (doxylamine succinate and pyridoxine hydrochloride) in direct conjunction with the proprietary name (DICLEGIS) where the proprietary name is featured in the opening sentence of the letter, as required by 21 CFR 201.10(g)(1).

Failure to Provide Adequate Directions for Use

We note that the letter does not appear to have been disseminated with the full FDA-approved product labeling for DICLEGIS, in violation of 21 CFR 201.100(d).

Conclusion and Requested Action

For the reasons discussed above, the letter misbrands DICLEGIS in violation of the FD&C Act, 21 U.S.C. 352(a) & 321(n). *Cf.* 21 CFR 202.1 (e)(5). Furthermore, Duchesnay did not comply with 21 CFR 201.10(g)(1) and it appears that Duchesnay also did not comply with 21 CFR 201.100(d).

OPDP requests that Duchesnay immediately cease the dissemination of violative promotional materials for DICLEGIS such as those described above. Please submit a written response to this letter on or before November 26, 2013, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for DICLEGIS that contain violations such as those described above, and explaining your plan for discontinuing use of such violative 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 # 3 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 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 promotional materials for DICLEGIS comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

Carrie Newcomer, PharmD
Regulatory Review Officer
Office of Prescription Drug Promotion

{See appended electronic signature page}

Twyla Thompson, PharmD
Team Leader
Office of Prescription Drug Promotion

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

/s/

CARRIE A NEWCOMER
11/12/2013

TWYLA N THOMPSON
11/12/2013