



TRANSMITTED BY FACSIMILE

ECR Pharmaceuticals, a wholly owned subsidiary of Valeant
Pharmaceuticals International
Attention: J. Michael Pearson, CEO Valeant Pharmaceuticals
International
400 Somerset Corporate Center
Bridgewater, NJ 08807

RE: ANDA 077273
TussiCaps[®] (hydrocodone polistirex and chlorpheniramine polistirex)
Extended-release Capsules CII¹
MA #86

WARNING LETTER

Dear Mr. Pearson:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a professional sales aid (DTUS3B) (sales aid) for TussiCaps[®] (hydrocodone polistirex and chlorpheniramine polistirex) Extended-release Capsules CII (TussiCaps) submitted by ECR Pharmaceuticals under cover of Form FDA 2253. The sales aid is false or misleading because it omits risk information, inadequately communicates the full indication for the drug, and presents unsubstantiated claims for TussiCaps. Thus, the sales aid misbrands TussiCaps 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); 321(n); 331(a); 21 CFR 1.21(a). Cf. 21 CFR 202.1(e)(3)(ii); (e)(5); (e)(7)(i). These violations are concerning from a public health perspective because they suggest that TussiCaps, a drug associated with a number of serious and potentially fatal risks, is safer than has been demonstrated.

Background

Below are the indication and summary of the most serious and most common risks associated with the use of TussiCaps.²

¹ The version of the TussiCaps PI that was approved when the piece cited in this letter was disseminated and the version referred to in this letter is dated March 3, 2009. However, a new version of the PI was approved on November 20, 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 cited in this letter.

According to the FDA-approved product labeling (PI), TussiCaps is indicated for relief of cough and upper respiratory symptoms associated with allergy or a cold in adults and children 6 years of age and older.

TussiCaps is associated with serious risks. Specifically, TussiCaps is contraindicated in patients with a known allergy or sensitivity to hydrocodone or chlorpheniramine, and in children less than 6 years of age due to the risk of fatal respiratory depression. The PI also includes warnings about respiratory depression, head injury and increased intracranial pressure, acute abdominal conditions, obstructive bowel disease, and pediatric use. In addition, the PI includes precautions regarding patients with narrow-angle glaucoma, asthma, or prostatic hypertrophy, elderly or debilitated patients, and patients with severely impaired hepatic or renal function, hypothyroidism, Addison's disease, or urethral stricture. Additionally, the PI indicates that TussiCaps is associated with drug abuse and dependence, and adverse reactions such as nausea and vomiting, sedation, drowsiness, mental clouding, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, dizziness, psychic dependence, mood changes, and dose-related respiratory depression which has been associated with death.

Omission of Risk Information

Promotional materials are misleading if they fail to reveal facts that are material in light of representations made or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials.

The four page sales aid is misleading because it includes numerous efficacy claims for TussiCaps, but fails to include **any** risk information about the product. We note that the bottom of the last page of the sales aid includes the following statements:

This brochure is the property of ECR Pharmaceuticals and is to remain in the representative's possession. Appropriate product labeling should accompany discussions with the healthcare professionals and distribution of product samples.

However, these statements do not mitigate the omission of risk information from the sales aid. By failing to present **any** information regarding the risks associated with TussiCaps, including serious and potentially fatal risks, the sales aid is misleading because it suggests that the drug is safer than has been demonstrated, and is especially concerning in its potential impact on the public health.

Inadequate Communication of Indication

The sales aid claims that TussiCaps is "[f]or the relief of cough and upper respiratory symptoms associated with colds or allergies." This claim is misleading because it fails to adequately communicate the full approved indication for TussiCaps. Specifically, the INDICATIONS AND USAGE section of the PI states the following (emphasis added):

TussiCaps[®] (hydrocodone polistirex and chlorpheniramine polistirex) extended-release capsules are indicated for relief of cough and upper respiratory symptoms associated with allergy or a cold **in adults and children 6 years of age and older.**

This misleading presentation is exacerbated by the image, on page two of the sales aid, of a coughing young child. As mentioned in the Background section above, TussiCaps is contraindicated in children less than 6 years of age due to the risk of fatal respiratory depression. The PI also indicates that caution should be exercised when administering TussiCaps to pediatric patients 6 years of age and older. We acknowledge that the bottom of the last page of the sales aid contains the statement, "**Usual Dosage:** One full-strength or half-strength capsule every 12 hours, depending on age, for patients six years of age and older" (emphasis in original). However, this does not mitigate the misleading impression.

Unsubstantiated Claims

The sales aid contains claims and presentations such as the following, found on page 3:

- The juxtaposition of the headline claim, "**Patient Preferred Capsule,**" in bold and large type set, with the image of two ivory TussiCaps capsules stamped with "ECR" on the caps and "HP/CP" over "5/4" and "10/8" on the bodies.

The following claims appear directly under the headline claim and image of TussiCaps capsules:

- "73% of adult prescription cough syrup users said they prefer capsules over liquid medications"^[3]
- "Small, easy to swallow capsule"
 - ✓ No unpleasant taste
 - ✓ Convenient
 - ✓ Accurate, without requiring measurement of a liquid
 - ✓ Not messy"

These claims and image are presented in conjunction with an additional image that depicts a transparent reclosable zip bag containing a bottle of red liquid medication, a spoon, cough drops, and various personal hygiene items. The bottom of the bag also contains a substantial amount of red liquid that appears to have leaked from the bottle of liquid medication.

The totality of these claims and presentations is misleading because it suggests that as a result of their capsule dosage form, patients specifically prefer TussiCaps capsules over oral liquid formulations. A study by Harris Interactive[®], is cited to support the patient preference claim for the TussiCaps dosage form. (No references are cited in support of the other claims and presentations.) Specifically, the cited study (b) (4) regarding dosage form preference (b) (4) is insufficient to support claims of patient preference for the capsule formulation of TussiCaps over liquid formulations (b) (4) that did not specifically evaluate TussiCaps compared to liquid

³ Harris Interactive[®] fielded the study on behalf of Covidien[®] from Jul. 30-Aug. 1, 2008, via its QuickQuery[®] online omnibus service. Interviewing a nationwide sample of 2,034 adults aged 18 and older, among which 983 have ever used prescription cough suppressant syrup. No estimates of theoretical sampling error can be calculated; a full methodology is available.

formulations. Therefore, the cited study is insufficient to support claims of patient preference for the capsule dosage form of TussiCaps over liquid formulations in the context of TussiCaps promotion. If you have evidence to support these claims and presentations regarding dosage form preference for TussiCaps, please submit it to FDA for review.

Conclusion and Requested Action

For the reasons discussed above, the sales aid misbrands TussiCaps within the meaning of the FD&C Act, and makes its distribution violative. 21 U.S.C. 352(a); 321(n); 331(a); 21 CFR 1.21(a). *Cf.* 21 CFR 202.1(e)(3)(ii); (e)(5); (e)(7)(i).

OPDP requests that ECR Pharmaceuticals immediately cease misbranding TussiCaps and/or cease introducing the misbranded drug into interstate commerce. Please submit a written response to this letter on or before August 10, 2015, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for TussiCaps that contain presentations such as those described above, and explaining your plan for discontinuing use of such materials, or, in the alternative, for ceasing distribution of TussiCaps. Because the violations described above are serious, we request, further, that your submission include a comprehensive plan of action to disseminate truthful, non-misleading, and complete corrective messages about the issues discussed in this letter to the audience(s) that received the violative promotional materials. In order to clearly identify the violative promotional piece(s) and/or activity and focus on the corrective message(s), OPDP recommends that corrective piece(s) include a description of the violative promotional pieces and/or activity, include a summary of the violative message(s), provide information to correct each of the violative message(s), and be free of promotional claims and presentations. To the extent possible, corrective messaging should be distributed using the same media, and generally for the same duration of time and with the same frequency that the violative promotional material was disseminated.

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 Amundson 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 #86 in addition to the ANDA 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 Warning 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 TussiCaps comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Failure to correct the violations discussed above may result in FDA regulatory action, including seizure or injunction, without further notice.

Sincerely,

{See appended electronic signature page}

Robert Dean, MBA, RAC
Division Director
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/

TWYLA N THOMPSON

07/27/2015

On behalf of ROBERT T DEAN