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Maternal Health Team Label Review

Date: June 25, 2008 **Date Consulted:** June 12, 2008

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To: Division of Dermatologic and Dental Products (DDDP)

Drug: Lice asphyxiator lotion, benzyl alcohol 5%; NDA 22-129

Subject: Pregnancy and Nursing Mothers labeling

Materials Reviewed: Pregnancy and Nursing Mothers subsections of Lice asphyxiator lotion labeling.

Consult Question: Please review sections of the proposed label as they relate to pregnancy and lactation.

INTRODUCTION

Sciele Pharma, Inc. had submitted a new drug application (NDA), to the Division of Dermatologic and Dental Products for Lice asphyxiator lotion, which is a lotion formulation of benzyl alcohol 5%. The sponsor's proposed indication is for the topical treatment of head lice (Pediculosis capitis).

On June 12, 2008, the DDDP consulted the Maternal Health Team (MHT) to review the Pregnancy and Nursing Mothers section of the package insert, and provide comment. Labeling recommendations were sent to the Division by e-mail on June 25, 2008. This review provides revisions to the sponsor's proposed Pregnancy and Nursing Mothers subsections of labeling for documentation in DFS.

BACKGROUND

The Maternal Health Team (MHT) is working to develop a more consistent and clinically useful approach to the Pregnancy and Nursing Mothers subsections of labeling. This approach complies with current regulations but incorporates "the spirit" of the Proposed Pregnancy and Lactation Labeling Rule (published on May 28, 2008).

As part of the labeling review, the MHT reviewer conducts a literature search to determine if relevant published pregnancy and lactation data are available that would add clinically useful information to the pregnancy and nursing mothers label subsections. In addition, the MHT presents available animal data, in the pregnancy subsection, in an organized, logical format that makes it as clinically relevant as possible for prescribers. This includes expressing animal data in terms of species exposed, timing and route of drug administration, dose expressed in terms of human dose equivalents (with the basis for calculation), and outcomes for dams and offspring. For nursing mothers, when animal data are available, only the presence or absence of drug in milk is considered relevant and presented in the label, not the amount.

This review provides revisions to the sponsor's proposed Pregnancy and Nursing Mothers subsections of Lice asphyxiator lotion labeling.

SUBMITTED MATERIAL

Sponsor's Proposed Pregnancy and Nursing Mothers Labeling

8.1 Pregnancy

Pregnancy Category B

(b) (4)



8.3 Nursing Mothers

It is not known whether benzyl alcohol is excreted in human milk. Caution should be exercised when 5% L.A. is administered to a nursing woman. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug for the mother.

RECOMMENDATIONS

Provided below are the MHT's recommended revisions to the sponsor's proposed labeling.

8.1 Pregnancy

Pregnancy Category B

There are no adequate and well-controlled studies with topical benzyl alcohol in pregnant women. Reproduction studies conducted in rats and rabbits were negative. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

No comparisons of animal exposure with human exposure are provided in this labeling due to the low systemic exposure noted in the clinical pharmacokinetic study [*See Clinical Pharmacology (12.3)*] which did not allow for determination of human AUC values that could be used for this calculation.

Pregnant rats were dosed with benzyl alcohol via subcutaneous injection at 100, 250, and 500 mg/kg/day. No teratogenic effects were noted at any dose. Maternal toxicity and decreased fetal weight occurred at 500 mg/kg/day. When pregnant rabbits received subcutaneous injections of benzyl alcohol at 100, 250, and 400 mg/kg/day, there were no teratogenic effects in offspring at any dose. In rabbits, maternal toxicity occurred at the two higher doses and was associated with decreased fetal weight at the highest dose.

8.3 Nursing Mothers

It is not known whether benzyl alcohol is excreted into human milk. Because some systemic absorption of topical benzyl alcohol may occur and because many drugs are excreted in human milk, caution should be exercised when TRADENAME is administered to a nursing woman.

CONCLUSIONS

While the Proposed Pregnancy and Lactation Labeling Rule, published May 2008, is in the clearance process, the MHT is structuring the Pregnancy and Nursing Mothers label information in a way that is in the spirit of the Proposed Rule while still complying with current regulations.

The goal of this restructuring is to make the pregnancy and lactation sections of labeling a more effective communication tool for clinicians.

The MHT's recommended labeling for Lice Asphyxiator lotion is provided on page 3 of this review.

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/s/

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1/21/2009 08:53:17 AM
MEDICAL OFFICER

The Division asked us to archive our labeling recommendations
in DFS.

Karen Feibus
1/21/2009 02:09:36 PM
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I concur with the content and recommendations in this
review.

Lisa Mathis
1/27/2009 09:51:23 AM
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