DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NOV 24 1999

TRANSMITTED VIA FACSIMILE

Carol Patterson, MS
Manager, Regulatory Affairs
Endo Pharmaceuticals Inc.
500 Endo Blvd.
Garden City, NY 11530

RE: NDA 20-612
Lidoderm (lidocaine patch 5%)
MACMIS ID #8491

Dear Ms. Paterson:

This letter is in reference to Endo Pharmaceuticals Inc.'s (Endo) submission, dated October 13, 1999, of promotional materials under cover of Form FDA 2253 for Lidoderm. This submission included a sales aid, identified as LD-1004. The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed the sales aid and has concluded that it is in violation of the Federal Food Drug and Cosmetic Act (Act) and its implementing regulations. Our specific objections follow:

Fair Balance

In general, promotional materials are misleading if they fail to include information about the risks associated with the use of a drug with a prominence and readability reasonably comparable to that of claims for the drug. We object to the lack of fair balance with respect to the content and presentation of risk information in this sales aid. The efficacy claims for Lidoderm are prominently presented, by way of numerous headers and bullets, in large print throughout the sales aid. In contrast, you frequently present the risk information in small sized type, confined to the bottom of selective pages. Moreover, selective pieces of Lidoderm risk information, including the drug's bolded warning, is presented in a manner that is difficult to read, taking into account the size and coloring of the type and the background on which it is presented. Consequently, we consider this sales aid to be lacking in fair balance. In addition, we object to your selective presentation of risk information for the following reasons:

- You present the statement, "Store and dispose of Lidoderm® patches out of the reach of children and pets," on the bottom of the last page of the sales aid. However, this selective presentation of the bolded warning does not sufficiently convey the importance of this

warning and the serious risks this product presents to children and pets. Under the bolded header, "Accidental Exposure in Children," the approved product labeling (PI) states, "Even a *used* Lidoderm patch contains a large amount of lidocaine (at least 665 mg). The potential exists for a small child or a pet to suffer serious adverse effects from chewing or ingesting a new or used Lidoderm patch...." Therefore, we consider this sales aid to be lacking in fair balance, because it does not sufficiently convey the serious risks that even a used Lidoderm patch presents if not stored and disposed of appropriately. Moreover, we consider claims regarding the ease of application and removal of the Lidoderm patch to be misleading without also prominently disclosing information concerning this important bolded drug warning. Therefore, DDMAC considers the claim, "easy to apply, easy to remove," adjacent to the headline "Simply," on two separate pages of the sales aid to be misleading, because it omits important contextual information concerning the bolded warning for Lidoderm, thereby minimizing this risk information.

- On page five of the sales aid you disclose, "Excessive dosing could result in increased absorption of lidocaine and high blood concentrations, leading to serious adverse effects." However, this selective presentation of Lidoderm's warning omits material fact concerning situations that may contribute to excessive dosing of Lidoderm, and is therefore, misleading. For instance, the PI states, "Excessive dosing by applying LIDODERM to larger areas or longer than the recommended wearing time could result in increased absorption of lidocaine and high blood concentrations, leading to serious adverse effects." (emphasis added).

- In addition, the presented content of the sales aid is lacking in fair balance, because important precautions and drug interactions associated with Lidoderm are not disclosed. For instance, the PI states, "Patients with severe hepatic disease are at a greater risk of developing toxic blood concentrations of lidocaine," and "Lidoderm should be used with caution in patients receiving Class I antiarrhythmic drugs...."

Contextual Information

- You present the claims "Preferred by 78% of patients vs placebo patch," and "88% of patients completed the Lidoderm phase of the study due to effective pain relief (vs 38% in placebo phase)." These claims are supported from the clinical study entitled, "Topical lidocaine patch relieves postherpetic neuralgia more effectively than a vehicle topical patch: results of an enriched enrollment study," listed as reference #2. We note that you disclose this was an enriched enrollment study. However, adequate context regarding the limitations of the study is not disclosed. Specifically, you omit the material fact that, "Limitations of enriched enrollment studies include the realization that the results are not generalizable to the entire population and the possibility that subjects may be able to identify the study treatment from placebo due to non-therapeutic features of treatment," as it is stated in discussion section of this clinical study. Therefore, we consider these efficacy claims misleading because they disclose favorable conclusions from a study, in the absence of qualifying contextual information concerning the study's limitations.

You should immediately cease distribution of this sales aid and other similar promotional materials, including information available on your worldwide website, which contain the same or similar claims or presentations. You should submit a written response on or before December 9, 1999, describing your intent and plans to comply with the above. Your letter should also include a list of materials discontinued and the date on which these materials were discontinued.

You should direct your response to the undersigned by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-42, Rm. 17B-17, 5600 Fishers Lane, Rockville, MD 20857. We remind you that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #8491 in addition to the NDA number.

Sincerely,

/S/

Spencer Salis, Pharm.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications