DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-372/S-008/S-010

Helsinn Healthcare SA
US Representative: August Consulting
Attention: Craig Lehmann, Pharm.D.
Authorized Representative
515 Capital of Texas Hwy, Suite #150
Austin, TX 78746

Dear Dr. Lehmann (US Agent):

Please refer to your supplemental new drug applications dated April 27, 2007, received May 4, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aloxi (palonosetron hydrochloride), 0.075 mg/1.5 mL Intravenous Injection.

We acknowledge receipt of your submissions dated April 27, 2007; June 21, 2007; June 27, 2008; June 28, 2007; July 11, 2007; July 18, 2007; July 27, 2007; September 6, 2007; October 9, 2007; October 31, 2007; November 2, 2007; November 5, 2007; December 6, 2007; January 14, 2008; February 7, 2008; February 8, 2008; February 19, 2008; February 20, 2007; February 21, 2008; February 22, 2008; and February 29, 2008.

These supplemental new drug applications provide for the use of Aloxi (palonosetron hydrochloride) 0.075 mg/1.5 mL intravenous injection for:

- S-008: the prevention of postoperative nausea and vomiting for up to 24 hours following surgery
- S-010: the removal of QT safety information currently found in the label

We completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the editorial revisions listed below.

Package Insert Label

- Delete the underlined numbering for 6.1, 6.2, 14.1, and 14.2 in the "FULL PRESCRIBING INFORMATION."
- In the "HIGHLIGHTS OF PRESCRIBING INFORMATION" section "INDICATIONS AND USAGE," add the words "(PONV) for up to 24 hours following surgery" after the first sentence to read "Prevention of postoperat ausea and vomiting (PONV) for up to 24 hours following surgery." Delete the word in the second sentence.
- In the "FULL PRESCRIBING INFORMATION" section 1.2 "Postoperative Nausea and Vomiting," add the words "(PONV) for up to 24 hours following surgery" at the end of the first sentence to read "Prevention of postoperative nausea and vomiting (PONV) for up to

- In the "FULL PRESCRIBING INFORMATION" section 14.2 "Postoperative Nausea and Vomiting," delete the words [redacted] and add "compared to" in the first paragraph following Table 6 [redacted] ron 0.075 mg reduced the severity of nausea compared to placebo."
- In the "FULL PRESCRIBING INFORMATION" section 14.2 "Postoperative Nausea and Vomiting," delete the word [redacted] and add "formally" in first paragraph following Table 6 to read "Analyses o [redacted] ary endpoints indicate that palonosetron 0.075 mg was numerically better than placebo, however, statistical significance was not formally demonstrated."
- In the section "Patient Information," delete the last bullet under "What is ALOXI used for?"

Container Label

- Revise the color scheme for the 0.075 mg/1.5 mL strength to ensure it is adequately differentiated from the 0.25 mg/5 mL strength.
- Revise the color scheme for the proprietary name so that the entire name is presented in one color font.
- Revise the color of the font utilized for the established name and product strength so that it provides adequate contrast against the grey backround.
- Increase the prominence of the established name and product strength.

Carton Labeling

- Revise the color scheme of the proprietary name so that the entire name is presented in one color font.
- Revise the color of the font utilized or the established name and product strength so that it provides adequate contrast against the grey backround.
- Increase the prominence of the established name and product strength.
- Eliminate the use of trailing zeroes.

We also acknowledge your submission dated February 29, 2008 in which you agreed to the following:

- Resolve the expression of palonosetron nomenclature and dosage strength on the carton label, container label, and in the package insert to present the milligram strength consistent with the established name, similar to other FDA-approved product labels.
- Include a "New Strength" banner on the principal display panel of the carton for period of up to approximately six months provided the you can exhaust product inventory which includes this banner which may take longer than 6 months.

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert). These revisions are terms of the approval of these applications. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission "**SPL for approved supplement NDA 21-372/S-008/S-010**."

Submit final printed carton and container labels that are identical to the submitted carton and immediate container labels dated October 9, 2007, except for including the revisions listed and the agreed upon revisions in your submission dated February 29, 2008, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005).* Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 21-372/S-008/S-010**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

All applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable. We are waiving the pediatric study requirement for ages 0 to 1 month of age because necessary studies are impossible or highly impractical because there are too few children in this age group to study. We are deferring submission of your pediatric study for ages 1 month to 16 years for this application because the drug is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric study required by section 505B(a) of the Food, Drug, and Cosmetic Act are required postmarketing study commitments. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Food, Drug, and Cosmetic Act. This commitment is listed below.

1. Deferred pediatric study under PREA to evaluate (1) the safety and tolerability of two doses of I.V. palonosetron for the prevention of postoperative nausea and vomiting, and (2) the efficacy of these two I.V. palonosetron doses to prevent postoperative nausea and vomiting.

   Final Report Submission: December 13, 2008

Submit final study reports to this NDA. For administrative purposes, all submissions related to this/these pediatric postmarketing study commitment(s) must be clearly designated "**Required Pediatric Study Commitments**".

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Gastroenterology Products and two copies of both the promotional materials and the package inserts directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Jagjit Grewal, Regulatory Project Manager, at (301) 796-0846.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., MPH
Deputy Division Director
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure: Package Insert Label

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

/s/

Joyce Korvick
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