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APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-372

Approval Letter(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-372

Helsinn Healthcare S.A.
c/o August Consulting
Attention: Craig Lehmann, Pharm. D.
515 Capital of Texas Highway, Suite 150
Austin, TX 78746

Dear Dr Lehmann:

Please refer to your new drug application (NDA) dated September 26, 2002, received September 27, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aloxi™ (palonosetron hydrochloride injection).

We acknowledge receipt of your submissions dated October 11 and November 21, 2002 and January 24, April 9, April 24, May 15, June 6, June 9, June 13, June 16, June 18, June 20, June 25, July 1, July 17, and July 22, 2003.

This new drug application provides for the use of Aloxi™ (palonosetron hydrochloride injection) for:
1) the prevention of acute nausea and vomiting associated with initial and repeat courses of moderately and highly emetogenic cancer chemotherapy, and
2) the prevention of delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

Please note that, based on the primary stability data submitted, we are granting a 24-month expiration period for this product. When additional stability data are available, an extension of the expiration period may be requested by submission of a prior approval supplemental new drug application.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert) and submitted labeling (carton label submitted June 25, 2003 and immediate container label submitted July 1, 2003). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-372.**" Approval of this submission by FDA is not required before the labeling is used.

FDA's Pediatric Rule [at 21 CFR 314.55/21 CFR 601.27] was challenged in court. On October 17, 2002, the court ruled that FDA did not have the authority to issue the Pediatric Rule and has barred FDA from enforcing it. Although the government decided not to pursue an appeal in the courts, it will work with Congress in an effort to enact legislation requiring pharmaceutical manufacturers to conduct appropriate pediatric clinical trials. In addition, third party interveners have decided to appeal the court's decision striking down the rule. Therefore, we encourage you to submit a pediatric plan that describes development of your product in the pediatric population where it may be used. Please be aware that whether or not this pediatric plan and subsequent submission of pediatric data will be required depends upon passage of legislation or the success of the third party appeal. In any event, we hope you will decide to submit a pediatric plan and conduct the appropriate pediatric studies to provide important information on the safe and effective use of this drug in the relevant pediatric populations.

The pediatric exclusivity provisions of FDAMA as reauthorized by the Best Pharmaceuticals for Children Act are not affected by the court's ruling. Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products. You should refer to the Guidance for Industry on Qualifying for Pediatric Exclusivity (available on our web site at www.fda.gov/cder/pediatric) for details. We acknowledge your June 26, 2003 "Proposed Pediatric Study Request" submitted under IND [redacted] We are reviewing your submission and will respond to your proposal in a separate letter. FDA generally does not consider studies submitted to an NDA before issuance of a Written Request as responsive to the Written Request. Applicants should obtain a Written Request before submitting pediatric studies to an NDA.

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 this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81). In addition, we request that you initiate a 15-day report [21 CFR 314.80(c)] for each of the following:

- All spontaneous reports of constipation requiring hospitalization or emergency room visit
- All spontaneous reports of possible complications of constipation such as obstruction, perforation, intestinal ulceration, toxic megacolon, ileus, or impaction resulting in hospitalization or emergency room visit
- All spontaneous reports of any cardiovascular adverse event

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics

qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www. fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Brian Strongin, R.Ph., M.B.A., Regulatory Project Manager at (301) 827-7473.

Sincerely,

{See appended electronic signature page}

Julie Beitz, M.D.
Deputy Director
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

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

/s/

Julie Beitz

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