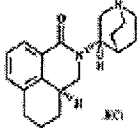


**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
21-372/S008/S010

CHEMISTRY REVIEW(S)

| | | | |
|---|---------------------------------|---|-----------------------------|
| Chemist Review: # 1 | | 1. Division: ONDQA Div. IV, Branch VIII | 2. NDA Number 21-372 |
| 3. Name and Address of Applicant: Helsinn Healthcare SA G915 Pambio-Noranco Lugano, Switzerland | | 4. Supplement(s): Number: SE1-008 Date(s): April 27 th , 2008 | |
| 5. Name of Drug: Aloxi (palonosetron•HCl) Injection | | 6. Nonproprietary name: Palonosetron injection | |
| 7. Supplement Provides new efficacy claim of prevention of post-operative (b) (4) nausea and vomiting up to (b) (4) (b) (4) and to provide a new package presentation (0.075 mg/1.5 mL in a 2-mL vial) | | 8. Amendment(s): | |
| 9. Pharmacological Category: Treatment of CINV and PONV | 10. How Dispensed: Rx | 11. Related Documents: NA | |
| 12. Dosage Form: I.V. injection | 13. Potency: 0.05 mg/mL | | |
| 14. Chemical Name and Structure: palonosetron•HCl | | | |
| <p>receptor. Chemically, palonosetron hydrochloride is: (3aS)-2-[(S)-1-Azabicyclo [2.2.2]oct-3-yl]-2,3,3a,4,5,6-hexahydro-1-oxo-1Hbenz[de]isoquinoline hydrochloride. The empirical formula is C₁₉H₂₄N₂O•HCl, with a molecular weight of 332.87. Palonosetron hydrochloride exists as a single isomer and has the following structural formula:</p> <div style="text-align: center;">  </div> | | | |

15. Comments: NDA 21-372/S-008, (b) (4) 010 were linked together for purpose of review. The CMC review will be attached to NDA 21-372/SE1-008, which proposes a new efficacy claim, namely the treatment of post-operative nausea and vomiting (PONV). The original NDA 21-372 was approved for use in the treatment of chemotherapy-induced nausea and vomiting (CINV). A CMC review is required for this supplement because the applicant is also proposing a new package presentation, designed to deliver a smaller dose for the PONV indication.

The original NDA provided for a 0.25 mg/5 mL dose (5 mL of a 0.05 mg/mL solution in a 5-mL glass vial sealed (b) (4)). This efficacy supplement proposes a 0.075 mg/1.5 mL dose (1.5 mL of a 0.05 mg/mL solution filled into a 2-mL glass vial (b) (4)).

The following CMC items are identical to those approved in original NDA 21-372:

- Drug substance manufacturer, method of manufacture, specifications, and stability
- Drug product formulation, method of manufacture (including sterilization), and manufacturing facility
- Drug product specifications (with the exception of the numerical value for fill volume) and test facility
- Composition of container closure system (b) (4)
- Stability protocol

The following CMC items are different for the new package presentation (21-372/S-008):

- Package presentation (container closure system size).
- (b) (4)

The application was consulted to the microbiology staff for review, and was found acceptable regarding sterility assurance (Review noted, no comments – NAI signed by Bryan Riley).

16. Conclusions and Recommendations: Recommend approval from the standpoint of CMC. Adequate information was provided regarding the new presentation of the drug product.

17. Name:
David Lewis, Ph.D., Chemist

Signature:

Date: February 29, 2008

18. Concurrence:
Hasmukh Patel, Ph.D., Branch Chief
ONDQA/DPME/Branch VIII

Signature:

Date:

4 Page(s) Withheld

✓ § 552(b)(4) Trade Secret /
Confidential

 § 552(b)(4) Draft Labeling

 § 552(b)(5) Deliberative Process

Withheld Track Number: Chemistry-21-372
5008

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

/s/

David Lewis

2/28/2008 05:17:01 PM

CHEMIST

Recommedn approval from the standpoint of CMC.

See memo (separate E-mail message) to be forwarded to

HFD-180

Hasmukh Patel

2/29/2008 08:26:20 AM

CHEMIST