CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

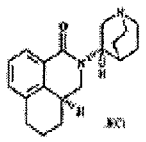
21-372/S008/S010

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 27th, 2008
5. Name of Drug: Aloxi (palonosetron•HCl) Injection		**6. Nonproprietary name:** Palonosetron injection
7. Supplement Provides new efficicacy 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

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-1*H*benz[*de*]isoquinoline hydrochloride. The empirical formula is $C_{19}H_{24}N_2O.HCl$, with a molecular weight of 332.87. Palonosetron hydrochloride exists as a single isomer and has the following structural formula:



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:	**Signature:**	**Date: February 29, 2008**
David Lewis, Ph.D., Chemist		

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

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 S008

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/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