

**CENTER FOR DRUG EVALUATION AND RESEARCH**

*APPLICATION NUMBER:*

**50-684 / S-045**

**50-750 / S-012**

**CHEMISTRY REVIEW(S)**

**NDA Supplement Review of Chemistry, Manufacturing and Controls  
Division of Anti-Infective Drug Products (HFD-520)**

1. **NDA NUMBER/SUPPLEMENT:** 50-684/SCF-045 Prior Approval (PA)

2. **REVIEW:** # 1

3. **DATE(s):** Letter Date: 27-May-05; Stamp Date: 02-Jun-05; Due Date: 02-Oct-05

4. **SUPPLEMENT PROVIDES FOR:**

The reformulation of ZOSYN<sup>®</sup> for Injection to contain edetate disodium dihydrate (EDTA) as a metal chelator and citric acid monohydrate as a buffer.

5. **PREVIOUS DOCUMENTS:** 50-684/SLR-044

6. **SUBMISSION(S) BEING REVIEWED:** 50-684/SCF-045

7. **NAME AND ADDRESS OF APPLICANT**

Wyeth Pharmaceuticals.  
P. O. Box 8299  
Philadelphia, PA 19101-8299  
(484) 865-3218  
Attn: David L. Urquhart  
Senior Regulatory Specialist  
Telephone: (484) 865-5958  
Fax: (484) 865-0028

8. **DRUG PRODUCT NAME:**

ZOSYN<sup>®</sup> (sterile piperacillin and tazobactam) for Injection

9. **PHARMACOLOGICAL CATEGORY:** Antibiotic

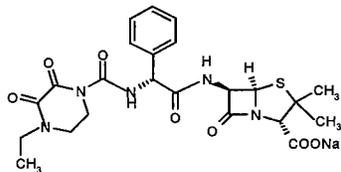
10. **DOSAGE FORM:** Injection Powder Lyophilized for Solution

11. **STRENGTH/POTENCY** 2.25 g, 3.375 g, 4.5 g, 40.5 g

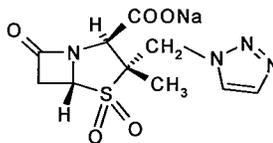
12. **ROUTE OF ADMINISTRATION:** Parenteral (Intravenous or Intramuscular)

13. **Rx/OTC DISPENSED:**  Rx  OTC

14. **CHEMICAL NAME, CHEMICAL STRUCTURE, MOLECULAR FORMULA, and MOLECULAR WEIGHT:** **STRUCTURE** Sodium (2S,5R,6R)-6-[(R)-2-(4-ethyl-2,3-dioxo-1-piperazine-carboxamido)-2-phenylacetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate; (2S,3S,5R)-3-methyl-7-oxo-3-(1H-1,2,3-triazol-1-ylmethyl)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate-4,4-dioxide;



$C_{23}H_{26}N_5NaO_7S$   
MW 539.55



$C_{10}H_{12}N_4NaO_5S$   
MW 322.28

15. **RELATED/SUPPORTING DOCUMENTS:** NDA 50-750-SCF-012, 50-750-SLR-011, 50-684/SLR-044,

**16. COMMENTS:**

Wyeth has assessed the effects of this change and presented data in support. The three exhibit batches complied with the approved test specifications for the drug product. Based on the information provided, the proposed reformulation of ZOSYN<sup>®</sup> for Injection to contain edetate disodium dihydrate (EDTA) as a metal chelator and citric acid monohydrate as a buffer should have no adverse effect on the identity, strength, quality, purity or potency of ZOSYN<sup>®</sup> (Piperacillin and Tazobactam for Injection) as these attributes relate to safety and effectiveness. Labeling comments relevant to CMC has been found acceptable. Other labeling revisions were previously reviewed only by biopharm and clinical review disciplines and similarly, the present revision of the PRECAUTIONS, Drug Interactions, Aminoglycosides sub-section of the label are deferred for review by biopharm and clinical.

**17. CONCLUSIONS AND RECOMMENDATIONS**

Recommendation is for approval of this supplement pending conclusion by Biopharm that changes are pharmaceutically and therapeutically equivalent.

<b>18. Name</b>	<b>Signature</b>	<b>Date Completed</b>
Milton J. Sloan, Ph. D. Review Chemist		23-Sep-05

**19. Concurrence:**

James D. Vidra, Ph. D.  
Chemistry Team Leader

CC: Archival: NDA 50-684  
HFD-520/PM/Samanta  
HFD-520/MO/Alexander

HFD-520/Chm/Sloan  
HFD-520/ChmTL/Vidra

**WITHHOLD 16 PAGE(S)**

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*Chemistry Review*

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/s/

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Milton Sloan

9/27/2005 02:09:01 PM

CHEMIST

Review team should provide comment on labeling revisions in  
Precautions subsection.

Jim Vidra

9/28/2005 12:10:01 PM

CHEMIST