


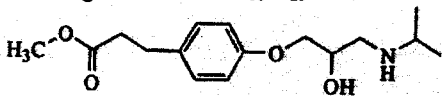
**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER**

**19-386/S-021**

**Chemistry Review(s)**

|  |   |   |   |
|--|---|---|---|
| <b>CHEMIST'S REVIEW</b>  |   | <b>1. ORGANIZATION</b><br>HFD-110   | <b>2. NDA Number</b><br>19-386  |
| <b>3. Name and Address of Applicant (City &amp; State)</b><br>Baxter Pharmaceutical Products Inc.<br>95 Spring Street<br>New Providence, NJ 07974  |   | <b>4. Supplement(s)</b><br><b>Number(s)</b> <b>Date(s)</b><br>SCF-021    10/24/02 |   |
| <b>5. Drug Name</b><br>Brevibloc   | <b>6. Nonproprietary Name</b><br>Esmolol HCl  |   | <b>7. Amendments &amp; Other (reports, etc) Dates</b><br>Amendment of 01/13/03<br>EA Exclusion Certification.<br><br>References: Approval letter of supplement #S018 of 2/16/01 & firm's proposal of 9/5/01       |
| <b>8. Supplement Provides For:</b><br>New Isotonic Formulation of Brevibloc Injection, 10 mg/mL in 10 mL vials with reduced overage of Active Ingredient from the approved % to overage % (as per phase 4 commitment). Also this submission provides for _____ vial in place of the currently used _____ vial.   |   |   |   |
| <b>9. Pharmacological Category</b><br>Anti-adrenergic (β receptor)   | <b>10. How Dispensed</b><br><input checked="" type="checkbox"/> Rx <input type="checkbox"/> OTC |   | <b>11. Related IND(s)/ NDA(s)/DMF(s)</b><br>Type II, DMF   |
| <b>12. Dosage Form(s)</b><br>Intravenous injection   | <b>13. Potency(ies)</b><br>10 mg/mL in 10 mL ready to use vials                                 |   |   |
| <b>14. Chemical Name and Structure</b><br>(±) methyl p-[2-hydroxy-(isopropylamino)propoxyl] hydrocinnamate hydrochloride<br><br>Molecular weight: 331.8    C <sub>16</sub> H <sub>25</sub> NO <sub>4</sub> .HCl<br><br><br><br>esmolol  |   |   | <b>15. Records/Reports</b><br><b>Current</b><br><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No<br><br><b>Reviewed</b><br><input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |
| <b>16. Comments:</b><br>Firm has provided the 3 months stability data in the ready to use new isotonic formulation containing NaCl, in the 10 mL vials. Firm has also provided the manufacturing formula and executed batch records of the three qualification batches in this supplement with reduced overage, of Brevibloc Injection 10 mg/mL in ready to use-10 mL vials. Firm has provided the revised labeling which reflects introduction of the isotonic agent, sodium chloride, USP, but immediate container label should also contain composition statement. Firm has now on our request, in an amendment of 01/11/03, sent the Environment Assessment Categorical Exclusion Certification.<br><br>Cont'd |   |   |   |
| <b>17. Conclusions and Recommendations</b><br>This P.A. supplement may be approved from the standpoint of chemistry. Refer also microbiological review of Dr. Pawar dated 01/22 /03 and draft labeling review of Dr. Shari Targum dated 01/09/03, filed with this supplement. The immediate container label should be revised. It should contain composition statement as it is in the current label.  |   |   |   |
| <b>18. REVIEWER</b>  |   |   |   |
| <b>Name</b><br>JV Advani   | <b>Signature</b>  |   | <b>Date Completed</b><br>Jan. 30, 2003  |
| Distribution: <input checked="" type="checkbox"/> Original Jacket <input checked="" type="checkbox"/> Reviewer <input checked="" type="checkbox"/> Division File <input checked="" type="checkbox"/> CSO   |   |   |   |

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/s/

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J. V. Advani  
2/14/03 06:53:31 AM  
CHEMIST

Kasturi Srinivasachar  
2/14/03 09:05:46 AM  
CHEMIST