

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

Approval Package for:

APPLICATION NUMBER:

76-500

Generic Name: Adenosine Injection USP, 3mg/mL
6mg/2mL Single-dose vials

Sponsor: Baxter Healthcare Corporation

Approval Date: June 16, 2004

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76-500

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**CENTER FOR DRUG
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RESEARCH**

APPLICATION NUMBER:

76-500

APPROVAL LETTER

ANDA 76-500

JUN 16 2004

Baxter Healthcare Corporation,
Anesthesia and Critical Care
Attention: Ivy Bautista
95 Spring Street
New Providence, NJ 07974

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated September 23, 2002, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Adenosine Injection USP, 3 mg/mL, packaged in 6 mg/2 mL single-dose vials.

Reference is also made to the Tentative Approval letter issued by this office on May 14, 2003, and to your amendments dated April 28, and May 25, 2004.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved. The Division of Bioequivalence has determined your Adenosine Injection USP, 3 mg/mL, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Adenocard[®] Injection, 3 mg/mL, of Fujisawa Healthcare, Inc.).

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert(s) directly to:

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

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications (HFD-42) with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,



Gary Buehler 6/16/04
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

76-500

**TENTATIVE APPROVAL
LETTER(S)**

ANDA 76-500

MAY 14 2003

Baxter Healthcare Corporation,
Anesthesia and Critical Care
Attention: Priya Jambhekar
95 Spring Street
New Providence, NJ 07974

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated September 23, 2002, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Adenosine Injection USP, 3 mg/mL, packaged in 6 mg/2 mL single-dose vials.

Reference is also made to your amendments dated February 24, and April 9, 2003.

We have completed the review of this abbreviated application and have concluded that based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted labeling. Although we are unable to grant final approval at this time due to patent issues noted below, the application is **tentatively approved**. This tentative approval is based upon information available to the Agency at this time, (i.e., information in your application and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacture and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention.

The reference listed drug product (RLD) upon which you have based your application, Adenocard® Injection of Fujisawa Healthcare, Inc., is currently subject to a period of patent protection. As noted in the agency's publication entitled Approved Drug Products with Therapeutic Equivalence Evaluations, the "Orange Book", U.S. patent 4,673,563 (the '563 patent) will expire on June 16, 2004. Your application contains a paragraph III certification to this patent under Section 505(j)(2)

(A) (vii) (III) of the Act stating that you will not market this drug product prior to the expiration of the '563 patent. Therefore, final approval of your application may not be made effective pursuant to 21 U.S.C. 355(j)(5)(B)(ii) of the Act until the '563 patent has expired, i.e., June 16, 2004.

In order to reactivate your application prior to final approval, please submit a MINOR AMENDMENT - FINAL APPROVAL REQUESTED 60 to 90 days prior to the date you believe that your application will be eligible for final approval. This amendment should provide a justification for the reasons you believe the ANDA is eligible for final approval, and it should also identify changes, if any, in the conditions under which the product was tentatively approved; i.e., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter that it represents a MINOR AMENDMENT - FINAL APPROVAL REQUESTED.

In addition to the amendment requested above, the agency may request at any time prior to the final date of approval that you submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your application, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this abbreviated application as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (cGMPs) are subject to Agency review before final approval of the application will be made. Such changes should be submitted as an amendment to the application and categorized as representing either "major" or "minor" changes. The amendment will be reviewed according to OGD policy in effect at the time of receipt. Your submission of multiple amendments prior to final approval may lead to a delay in the issuance of the final approval letter.

Please note that this drug product may not be marketed without final agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under Section 501 of the Act and 21 U.S.C. 331(d). Also, until the agency issues the final approval letter, this drug product will not be deemed approved for marketing under

21 U.S.C. 355 and will not be listed in the "Orange Book". Furthermore, should you believe that there are grounds for issuing the final approval letter prior to June 16, 2004, you should amend your application accordingly.

For further information on the status of this application, or prior to submitting additional amendments, please contact Stanley Shepperson, Pharm.D., Project Manager, at 301-827-5849.

Sincerely yours,



Gary Buehler 5/14/03
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

76-500

FINAL PRINTED LABELING

APPROVED
Adenosine Injection
For Rapid Bolus Intravenous Use
Rx only

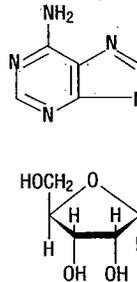
Adenosine Injection

For Rapid Bolus Intravenous Use

Rx only

DESCRIPTION

Adenosine is an endogenous nucleoside occurring in all cells of the body. It is chemically 6-amino-9-β-D-ribofuranosyl-9-H-purine and has the following structural formula:



$C_{10}H_{13}N_5O_4$

267.24

Adenosine is a white crystalline powder. It is soluble in water and practically insoluble in alcohol. Solubility increases by warming and lowering the pH. Adenosine is not chemically related to other antiarrhythmic drugs. Adenosine injection is a sterile, nonpyrogenic solution for rapid bolus intravenous injection. Each mL contains 3 mg adenosine and 9 mg sodium chloride in Water for Injection. The pH of the solution is between 4.5 and 7.5.

CLINICAL PHARMACOLOGY

Mechanism of Action

Adenosine slows conduction time through the A-V node, can interrupt the reentry pathways through the A-V node, and can restore normal sinus rhythm in patients with paroxysmal supraventricular tachycardia (PSVT), including PSVT associated with Wolff-Parkinson-White Syndrome.

Adenosine is antagonized competitively by methylxanthines such as caffeine and theophylline, and potentiated by blockers of nucleoside transport such as dipyridamole. Adenosine is not blocked by atropine.

Hemodynamics

The intravenous bolus dose of 6 or 12 mg adenosine usually has no systemic hemodynamic effects. When larger doses are given by infusion, adenosine decreases blood pressure by decreasing peripheral resistance.

Pharmacokinetics

Intravenously administered adenosine is rapidly cleared from the circulation via cellular uptake, primarily by erythrocytes and vascular endothelial cells. This process involves a specific transmembrane nucleoside carrier system that is reversible, nonconcentrative, and bidirectionally symmetrical. Intracellular adenosine is rapidly metabolized either via phosphorylation to adenosine monophosphate by adenosine kinase, or via deamination to inosine by adenosine deaminase in the cytosol. Since adenosine kinase has a lower K_m and V_{max} than adenosine deaminase, deamination plays a significant role only when cytosolic adenosine saturates the phosphorylation pathway. Inosine formed by deamination of adenosine can leave the cell intact or can be degraded to hypoxanthine, xanthine, and ultimately uric acid. Adenosine monophosphate formed by phosphorylation of adenosine is incorporated into the high-energy phosphate pool. While extracellular adenosine is primarily cleared by cellular uptake with a half-life of less than 10 seconds in whole blood, excessive amounts may be deaminated by an ecto-form of adenosine deaminase. As adenosine requires no hepatic or renal function for its activation or inactivation, hepatic and renal failure would not be expected to alter its effectiveness or tolerability.

Clinical Trial Results

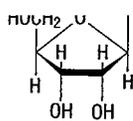
In controlled studies in the United States, bolus doses of 3, 6, 9, and 12 mg were studied. A cumulative 60% of patients with paroxysmal supraventricular tachycardia had converted to normal sinus rhythm within one minute after an intravenous bolus dose of 6 mg Adenosine (some converted on 3 mg and failures were given 6 mg), and a cumulative 92% converted after a bolus dose of 12 mg. Seven to sixteen percent of patients converted after 1-4 placebo bolus injections. Similar responses were seen in a variety of patient subsets, including those using or not using digoxin, those with Wolff-Parkinson-White Syndrome, males, females, blacks, Caucasians, and Hispanics.

Adenosine is not effective in converting rhythms other than PSVT, such as atrial flutter, atrial fibrillation, or ventricular tachycardia, to normal sinus rhythm. To date, such patients have not had adverse consequences following administration of adenosine.

INDICATIONS AND USAGE

Intravenous adenosine injection is indicated for the following:

Conversion to sinus rhythm of paroxysmal supraventricular tachycardia (PSVT), including that associated with accessory bypass tracts (Wolff-Parkinson-White Syndrome). When clinically



Adenosine is a white crystalline powder. It is soluble in water and practically insoluble in alcohol. Solubility increases by warming and lowering the pH. Adenosine is not chemically related to other antiarrhythmic drugs. Adenosine injection is a sterile, nonpyrogenic solution for rapid bolus intravenous injection. Each mL contains 3 mg adenosine and 9 mg sodium chloride in Water for Injection. The pH of the solution is between 4.5 and 7.5.

CLINICAL PHARMACOLOGY

Mechanism of Action

Adenosine slows conduction time through the A-V node, can interrupt the reentry pathways through the A-V node, and can restore normal sinus rhythm in patients with paroxysmal supraventricular tachycardia (PSVT), including PSVT associated with Wolff-Parkinson-White Syndrome.

Adenosine is antagonized competitively by methylxanthines such as caffeine and theophylline, and potentiated by blockers of nucleoside transport such as dipyridamole. Adenosine is not blocked by atropine.

Hemodynamics

The intravenous bolus dose of 6 or 12 mg adenosine usually has no systemic hemodynamic effects. When larger doses are given by infusion, adenosine decreases blood pressure by decreasing peripheral resistance.

Pharmacokinetics

Intravenously administered adenosine is rapidly cleared from the circulation via cellular uptake, primarily by erythrocytes and vascular endothelial cells. This process involves a specific transmembrane nucleoside carrier system that is reversible, nonconcentrative, and bidirectionally symmetrical. Intracellular adenosine is rapidly metabolized either via phosphorylation to adenosine monophosphate by adenosine kinase, or via deamination to inosine by adenosine deaminase in the cytosol. Since adenosine kinase has a lower K_m and V_{max} than adenosine deaminase, deamination plays a significant role only when cytosolic adenosine saturates the phosphorylation pathway. Inosine formed by deamination of adenosine can leave the cell intact or can be degraded to hypoxanthine, xanthine, and ultimately uric acid. Adenosine monophosphate formed by phosphorylation of adenosine is incorporated into the high-energy phosphate pool. While extracellular adenosine is primarily cleared by cellular uptake with a half-life of less than 10 seconds in whole blood, excessive amounts may be deaminated by an ecto-form of adenosine deaminase. As adenosine requires no hepatic or renal function for its activation or inactivation, hepatic and renal failure would not be expected to alter its effectiveness or tolerability.

Clinical Trial Results

In controlled studies in the United States, bolus doses of 3, 6, 9, and 12 mg were studied. A cumulative 60% of patients with paroxysmal supraventricular tachycardia had converted to normal sinus rhythm within one minute after an intravenous bolus dose of 6 mg Adenosine (some converted on 3 mg and failures were given 6 mg), and a cumulative 92% converted after a bolus dose of 12 mg. Seven to sixteen percent of patients converted after 1-4 placebo bolus injections. Similar responses were seen in a variety of patient subsets, including those using or not using digoxin, those with Wolff-Parkinson-White Syndrome, males, females, blacks, Caucasians, and Hispanics.

Adenosine is not effective in converting rhythms other than PSVT, such as atrial flutter, atrial fibrillation, or ventricular tachycardia, to normal sinus rhythm. To date, such patients have not had adverse consequences following administration of adenosine.

INDICATIONS AND USAGE

Intravenous adenosine injection is indicated for the following:

Conversion to sinus rhythm of paroxysmal supraventricular tachycardia (PSVT), including that associated with accessory bypass tracts (Wolff-Parkinson-White Syndrome). When clinically advisable, appropriate vagal maneuvers (e.g., Valsalva maneuver), should be attempted prior to adenosine administration.

It is important to be sure the adenosine solution actually reaches the systemic circulation (see **DOSAGE AND ADMINISTRATION**).

Adenosine does not convert atrial flutter, atrial fibrillation, or ventricular tachycardia to normal sinus rhythm. In the presence of atrial flutter or atrial fibrillation, a transient modest slowing of ventricular response may occur immediately following adenosine administration.

CONTRAINDICATIONS

Intravenous adenosine injection is contraindicated in:

1. Second- or third-degree A-V block (except in patients with a functioning artificial pacemaker).
2. Sinus node disease, such as sick sinus syndrome or symptomatic bradycardia (except in patients with a functioning artificial pacemaker).
3. Known hypersensitivity to adenosine.

WARNINGS

Heart Block

Adenosine injection exerts its effect by decreasing conduction through the A-V node and may produce a short lasting first-, second- or third-degree heart block. Appropriate therapy should be instituted as needed. Patients who develop high-level block on one dose of adenosine should not be given additional doses. Because of the very short half-life of adenosine, these effects are generally self-limiting.

Transient or prolonged episodes of asystole have been reported with fatal outcomes in some cases. Rarely, ventricular fibrillation has been reported following adenosine administration, including both resuscitated and fatal events. In most instances, these cases were associated with the concomitant use of digoxin and, less frequently with digoxin and verapamil. Although no causal relationship or drug-drug interaction has been established, adenosine should be used with caution in patients receiving digoxin or digoxin and verapamil in combination. Appropriate resuscitative measures should be available.

Arrhythmias at Time of Conversion

At the time of conversion to normal sinus rhythm, a variety of new rhythms may appear on the electrocardiogram. They generally last only a few seconds without intervention, and may take the form of premature ventricular contractions, atrial premature contractions, sinus bradycardia, sinus tachycardia, skipped beats, and varying degrees of A-V nodal block. Such findings were seen in 55% of patients.

Bronchoconstriction

Adenosine is a respiratory stimulant (probably through activation of carotid body chemoreceptors) and intravenous administration in man has been shown to increase minute ventilation (V_e) and reduce arterial PCO_2 causing respiratory alkalosis.

Adenosine administered by inhalation has been reported to cause bronchoconstriction in asthmatic patients, presumably due to mast cell degranulation and histamine release. These effects have not been observed in normal subjects. Adenosine has been administered to a limited number of patients with asthma and mild to moderate exacerbation of their symptoms has been reported. Respiratory compromise has occurred during adenosine infusion in patients with obstructive pulmonary disease. Adenosine should be used with caution in patients with obstructive lung disease not associated with

bronchoconstriction (e.g., emphysema, bronchitis, etc.) and should be avoided in patients with bronchoconstriction or bronchospasm (e.g., asthma). Adenosine should be discontinued in any patient who develops severe respiratory difficulties.

PRECAUTIONS

Drug Interactions

Intravenous adenosine has been effectively administered in the presence of other cardioactive drugs, such as quinidine, beta-adrenergic blocking agents, calcium channel blocking agents, and angiotensin converting enzyme inhibitors, without any change in the adverse reaction profile. Digoxin and verapamil use may be rarely associated with ventricular fibrillation when combined with adenosine (see **WARNINGS**). Because of the potential for additive or synergistic depressant effects on the SA and AV nodes, however, adenosine should be used with caution in the presence of these agents. The use of adenosine in patients receiving digitalis may be rarely associated with ventricular fibrillation (see **WARNINGS**).

The effects of adenosine are antagonized by methylxanthines such as caffeine and theophylline. In the presence of these methylxanthines, larger doses of adenosine may be required or adenosine may not be effective. Adenosine effects are potentiated by dipyridamole. Thus, smaller doses of adenosine may be effective in the presence of dipyridamole. Carbamazepine has been reported to increase the degree of heart block produced by other agents. As the primary effect of adenosine is to decrease conduction through the A-V node, higher degrees of heart block may be produced in the presence of carbamazepine.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies in animals have not been performed to evaluate the carcinogenic potential of adenosine. Adenosine was negative for genotoxic potential in the Salmonella (Ames Test) and Mammalian Microsome Assay.

Adenosine, however, like other nucleosides at millimolar concentrations present for several doubling times of cells in culture, is known to produce a variety of chromosomal alterations. Fertility studies in animals have not been conducted with adenosine.

Pregnancy Category C

Animal reproduction studies have not been conducted with adenosine; nor have studies been performed in pregnant women. As adenosine is a naturally occurring material, widely dispersed throughout the body, no fetal effects would be anticipated. However, since it is not known whether adenosine can cause fetal harm when administered to pregnant women, adenosine should be used during pregnancy only if clearly needed.

Pediatric Use

No controlled studies have been conducted in pediatric patients to establish the safety and efficacy of adenosine for the conversion of paroxysmal supraventricular tachycardia (PSVT). However, intravenous adenosine has been used for the treatment of PSVT in neonates, infants, children and adolescents (see **DOSAGE AND ADMINISTRATION**).¹

Geriatric Use

Clinical studies of adenosine did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between elderly and younger patients. In general, adenosine in geriatric patients should be used with caution since this population may have a diminished cardiac function, nodal dysfunction, concomitant diseases or drug therapy that may alter hemodynamic function and produce severe bradycardia or AV block.

ADVERSE REACTIONS

The following reactions were reported with intravenous adenosine used in controlled U.S. clinical trials. The placebo group had a less than 1% rate of all of these reactions.

Cardiovascular	Facial flushing (18%), headache (2%), sweating, palpitations, chest pain, hypotension (less than 1%).
Respiratory	Shortness of breath/dyspnea (12%), chest pressure (7%), hyperventilation, head pressure (less than 1%).
Central Nervous System	Lightheadedness (2%), dizziness, tingling in arms, numbness (1%), apprehension, blurred vision, burning sensation, heaviness in arms, neck and back pain (less than 1%).
Gastrointestinal	Nausea (3%), metallic taste, tightness in throat, pressure in groin (less than 1%).

Also, in post-market clinical experience with adenosine, cases of prolonged asystole, ventricular tachycardia, ventricular fibrillation, transient increase in blood pressure, bradycardia, atrial fibrillation, and bronchospasm, in association with adenosine use, have been reported (see **WARNINGS**).

OVERDOSAGE

The half-life of adenosine injection is less than 10 seconds. Thus, adverse effects are generally rapidly self-limiting. Treatment of any prolonged adverse effects should be individualized and be directed toward the specific effect. Methylxanthines, such as caffeine and theophylline, are competitive antagonists of adenosine.

DOSAGE AND ADMINISTRATION

For rapid bolus intravenous use only.

Adenosine injection should be given as a rapid bolus by the peripheral intravenous route. To be certain the solution reaches the systemic circulation, it should be administered either directly into a vein or, if given into an IV line, it should be given as close to the patient as possible and followed by a rapid saline flush.

Adult Patients

The dose recommendation is based on clinical studies with peripheral venous bolus dosing. Central venous (CVP or other) administration of adenosine has not been systematically studied.

The recommended intravenous doses for adults are as follows:

Initial dose: 6 mg given as a rapid intravenous bolus (administered over a 1 to 2 second period).

Repeat administration: If the first dose does not result in elimination of the supraventricular tachycardia within 1 to 2 minutes, 12 mg should be given as a rapid intravenous bolus. This 12 mg dose may be repeated a second time if required.

Pediatric Patients

The dosages used in neonates, infants, children and adolescents were equivalent to those administered to adults on a weight basis.

Pediatric Patients with a Body Weight < 50 kg:

Initial dose: Give 0.05 to 0.1 mg/kg as a rapid IV bolus given either centrally or peripherally. A saline flush should follow.

Repeat administration: If conversion of PSVT does not occur within 1 to 2 minutes, additional bolus injections of adenosine can be administered at incrementally higher doses, increasing the amount given by 0.05 to 0.1 mg/kg. Follow each bolus with a saline flush. This process should continue until sinus rhythm is established or a maximum single dose of 0.3 mg/kg is used.

Pediatric Patients with a Body Weight ≥ 50 kg:

Administer the adult dose.

Doses greater than 12 mg are not recommended for adult and pediatric patients.

NOTE: Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

HOW SUPPLIED

Adenosine injection is supplied as a sterile, non-pyrogenic solution in normal saline.

ADVERSE REACTIONS

The following reactions were reported with intravenous adenosine used in controlled U.S. clinical trials. The placebo group had a less than 1% rate of all of these reactions.

Cardiovascular	Facial flushing (18%), headache (2%), sweating, palpitations, chest pain, hypotension (less than 1%).
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Pediatric Patients with a Body Weight < 50 kg:

Initial dose: Give 0.05 to 0.1 mg/kg as a rapid IV bolus given either centrally or peripherally. A saline flush should follow.

Repeat administration: If conversion of PSVT does not occur within 1 to 2 minutes, additional bolus injections of adenosine can be administered at incrementally higher doses, increasing the amount given by 0.05 to 0.1 mg/kg. Follow each bolus with a saline flush. This process should continue until sinus rhythm is established or a maximum single dose of 0.3 mg/kg is used.

Pediatric Patients with a Body Weight ≥ 50 kg:

Administer the adult dose.

Doses greater than 12 mg are not recommended for adult and pediatric patients.

NOTE: Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

HOW SUPPLIED

Adenosine injection is supplied as a sterile, non-pyrogenic solution in normal saline.

NDC 10019-063-03 6 mg/2 mL (3 mg/mL) in 2 mL flip-top vials, packaged in shelf packs of ten.

NDC 10019-063-06 6 mg/2 mL (3 mg/mL) in a 2 mL disposable glass syringe, packaged in shelf packs of five.

Storage

Store at 20°-25°C (68°-77°F), excursions permitted to 15°-30°C (59°-86°F). [See USP Controlled Room Temperature.]

DO NOT REFRIGERATE as crystallization may occur. If crystallization has occurred, dissolve crystals by warming to room temperature. The solution must be clear at the time of use.

Contains no preservatives. Discard unused portion.

REFERENCE

1. Paul T. Pfammatter. J-P. Adenosine: an effective and safe antiarrhythmic drug in pediatrics. Pediatric Cardiology 1997; 18:118-126.

Baxter

Manufactured for

Baxter Healthcare Corporation

Deerfield, IL 60015 USA

By: Baxter Pharmaceutical Solutions LLC

Bloomington, IN 47403

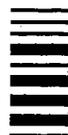
For Product Inquiry 1-800-ANA-DRUG (1-800-282-3674)

Revised April 2004

MLT-16/2.0

460-360-02

3-848-1808



ADENOSINE INJECTION

3 mg/mL in 2 mL vials

10 x 2 mL Vials Carton

460-359-01

NDC 10019-063-03

Adenosine Injection

6 mg/2 mL (3 mg/mL)
For Rapid Bolus Intravenous Use
10 x 2 mL Single Dose Vials

Each mL contains: Adenosine 3 mg and sodium chloride 9 mg in Water for Injection q.s. The pH of the solution is between 4.5 and 7.5.

Usual Dosage: See package insert.

Store at 20°-25°C (68°-77°F) (See USP Controlled Room Temperature).

DO NOT REFRIGERATE as crystallization may occur. If crystallization has occurred, dissolve crystals by warming to room temperature. The solution must be clear at the time of use.

Contains no preservatives.
Discard unused portion.



Lot: 460 - 359 - 01

Exp.:

NDC 10019-063-03

Adenosine Injection

6 mg/2 mL (3 mg/mL)
For Rapid Bolus Intravenous Use
10 x 2 mL Single Dose Vials
Sterile, Nonpyrogenic
DO NOT REFRIGERATE

NDC 10019-063-03

Adenosine Injection

6 mg/2 mL (3 mg/mL) & only
For Rapid Bolus Intravenous Use
10 x 2 mL Single Dose Vials
Sterile, Nonpyrogenic
Baxter
Manufactured by
Baxter Healthcare Corporation
Deerfield, IL 60015 USA

NDC 10019-063-03

Adenosine Injection

6 mg/2 mL (3 mg/mL)
For Rapid Bolus Intravenous Use
10 x 2 mL Single Dose Vials
Sterile, Nonpyrogenic
DO NOT REFRIGERATE

460-359-01 Adenosine 6 mg/2 mL (3 mg/mL), 10 x 2 mL Vials Carton
Size: 3" x 1 3/16" x 2"
USA
Submission - 1
2/6/2003

Approved by:

Baxter Packaging _____ Date _____

Baxter QA _____ Date _____

PMS 199 Fire Red = Horizontal Bands with Drop Out White Type.

PMS 287 Baxter Blue = All Other Text, Bar Code and Logo.

Multi-Color Stock Number = Prints in PMS 199 and 287.

Guide Lines = DO NOT PRINT.

Dotted Lines = Indicate Unvarnished Area. DO NOT PRINT.

CONTAINER LABEL

APPROVED

NDC 100310019563027
Adenosine Injection
6 mg/2 mL
(3 mg/mL) R only
For Rapid Bolus Intravenous Use
2 mL Single Dose Vial
DO NOT REFRIGERATE
See Package Insert
Baxter Healthcare Corp.
Deerfield, IL 60015 USA
3-847-1808 462-358-01
||| 78 10 11 |||
||| 78 10 11 |||
(01100310019563027)

Lot: 16
Exp:

PACKAGE INSERT

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

76-500

CSO LABELING REVIEW(S)

(this supersedes the tentative approval summary dated 5-19-04)

**APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number: 76-500

Date of Submission: May 25, 2004

Applicant's Name: Baxter Healthcare Corporation

Established Name: Adenosine Injection USP, 3 mg/mL 2 mL single dose vials

BASIS OF APPROVAL:

Patent Data - 19-937

No	Expiration	Use Code	Use	File
4673563	6-16-04	U-38	Treatment of paroxysmal supraventricular tachycardia	III

Exclusivity Data - 19-937

Code/sup	Expiration	Use Code	Description	Labeling Impact
None			There is no unexpired exclusivity for this product	

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? No - Tentative Approval

Container Labels: 2 mL

Satisfactory in FPL as of May 25, 2004 submission [v T90201].

Carton Labeling: 10 x 2 mL

Satisfactory in FPL as of February 24, 2003 submission [v 2.1].

Professional Package Insert Labeling:

Satisfactory in FPL as of May 25, 2004 submission [v T90201 - rev 4-04].

Revisions needed post-approval: None

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Adenocard®

NDA Number: 19-937

NDA Drug Name: Adenocard® (adenosine injection)

NDA Firm: Fujisawa

Date of Approval of NDA Insert and supplement # 4-20-99 (S-015):

Has this been verified by the MIS system for the NDA? YES

Was this approval based upon an OGD labeling guidance? NO

Basis of Approval for the Container Labels: side-by-sides

Basis of Approval for the Carton Labeling: side-by-sides

Other Comments Firm notified that if they so choose they may put "USP" on their labels and labeling for this ANDA and ANDA 76-501 for Adenosine Injection in syringes.

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N/A
Different name than on acceptance to file letter?		X	

Is this product a USP item? If so, USP supplement in which verification was assured. USP 27	X		
Is this name different than that used in the Orange Book?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? NO.		X	
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?		X	
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			X
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			X
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		X	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			X
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			X
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.	X		

NOTE TO THE CHEMIST:

The firm has revised their storage temperature recommendations to read "Store at 20 - 25°C (68 - 77°F), excursions permitted to 15° - 30°C (59° - 86°F). [See USP Controlled Room Temperature]. Does the submitted stability data support these storage temperature recommendations?

FOR THE RECORD: (portions taken from previous review)

1. Review based on the labeling of Adenocard®, revised 2-99; approved 4-20-99. This is NDA 19-937/S-015
2. Patent/ Exclusivities

There is one patent - 4673563 - which expires 6-16-04. The firm has certified PIII to this patent. There are no exclusivities.
3. Storage Conditions:
NDA - Store at controlled room temperature 15°-30°C (59°-86°F).
ANDA – [carton] - Store at 20°-25°C (68°-77°F)[See USP Controlled Room Temperature] – [insert] - Store at 20°-25°C (68°-77°F), excursions permitted to 15° -30°C (59° - 86°F). [See USP Controlled Room Temperature].
USP - Preserve in a single-dose container, preferably of Type I glass.
4. Product Line:
The innovator markets their product in 10 x 2 mL vials and 5 x 2 mL and 5 x 4 mL disposable syringes
The applicant proposes to market their product in 10 x 2 mL vials (ANDA 76-500) and 5 x 2 mL syringes (ANDA 76-501)
5. Inactive Ingredients:
The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing in section 4 (p 12, Volume 1.1).
6. Baxter is the manufacturer (p 179 v 1.2 section 9).
7. The vials are made of ~~---~~ Type 1 glass and they have green flip-off caps (p 487 v 1.4)..
8. This ANDA shares an insert with ANDA 76-501 which is for the syringes. Both must be approved together or the insert has to be revised

Date of Review: 6-2-04

Date of Submission: 5-25-04

Primary Reviewer: Adolph Vezza

Date:

6/8/04

Team Leader: Captain Lillie Golson

Date:

6/8/04

cc: ANDA: 76-500
DUP/DIVISION FILE
HFD-613/AVezza/LGolson (no cc)
aev/6/2/04|V:FIRMSAMBAXTER\LTRS&REV\76500.APL
Review

*Superseded by AP Summary dated
(this supersedes the TA Summary dated 3/24/03)*

**TENTATIVE APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number: 76-500

Date of Submission: April 28, 2004

Applicant's Name: Baxter Healthcare Corporation

Established Name: Adenosine Injection USP, 3 mg/mL 2 mL single dose vials

BASIS OF APPROVAL:

Patent Data - 19-937

No	Expiration	Use Code	Use	File
4673563	6-16-04	U-38	Treatment of paroxysmal supraventricular tachycardia	III

Exclusivity Data - 19-937

Code/sup	Expiration	Use Code	Description	Labeling Impact
None			There is no unexpired exclusivity for this product	

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? No - Tentative Approval

Container Labels: 2 mL

Satisfactory in FPL as of September 23, 2002 submission [v 1.1] [only 4 labels].

Carton Labeling: 10 x 2 mL

Satisfactory in FPL as of February 24, 2003 submission [v 2.1].

Professional Package Insert Labeling:

Satisfactory in draft as of April 24, 2004 submission [v 2.1].

Revisions needed post-approval:

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Adenocard®

NDA Number: 19-937

NDA Drug Name: Adenocard® (adenosine injection)

NDA Firm: Fujisawa

Date of Approval of NDA Insert and supplement # 4-20-99 (S-015):

Has this been verified by the MIS system for the NDA? YES

Was this approval based upon an OGD labeling guidance? NO

Basis of Approval for the Container Labels: side-by-sides

Basis of Approval for the Carton Labeling: side-by-sides

Other Comments I spoke to Ivy Bautista of the firm on 5-18-04 and requested they send in 12 FPL container labels and carton labeling for this application. They will comply.

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 27	X		

Is this name different than that used in the Orange Book?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? NO.		X	
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?		X	
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			X
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			X
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		X	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			X
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			X
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.	X		

NOTE TO THE CHEMIST:

The firm has revised their storage temperature recommendations to read "Store at 20 - 25° 77°F), excursions permitted to 15° - 30°C (59° - 86°F). [See USP Controlled Room Temperature] Does the submitted stability data support these storage temperature recommendations?

See review #2
item 32.
B.M

FOR THE RECORD: (portions taken from previous review)

1. Review based on the labeling of Adenocard®, revised 2-99; approved 4-20-99. This is NDA 19-937/S-015
2. Patent/ Exclusivities
There is one patent - 4673563 - which expires 6-16-04. The firm has certified PIII to this patent. There are no exclusivities.
3. Storage Conditions:
NDA - Store at controlled room temperature 15°-30°C (59°-86°F).
ANDA - [carton] - Store at 20°-25°C (68°-77°F)[See USP Controlled Room Temperature] - [insert] - Store at 20°-25°C (68°-77°F), excursions permitted to 15° -30°C (59° - 86°F). [See USP Controlled Room Temperature].
USP - Preserve in a single-dose container, preferably of Type I glass.
4. Product Line:
The innovator markets their product in 10 x 2 mL vials and 5 x 2 mL and 5 x 4 mL disposable syringes
The applicant proposes to market their product in 10 x 2 mL vials (ANDA 76-500) and 5 x 2 mL syringes (ANDA 76-501)
5. Inactive Ingredients:
The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing in section 4 (p 12, Volume 1.1).
6. Baxter is the manufacturer (p 179 v 1.2 section 9).
7. The vials are made of Type 1 glass and they have green flip-off caps (p 487 v 1.4)..
8. This ANDA shares an insert with ANDA 76-501 which is for the syringes. Both must be approved together or the insert has to be revised

Date of Review: 5-17-04

Date of Submission: 4-28-04

Primary Reviewer: Adolph Vezza

Date:

Team Leader: Captain Lillie Golson

Date:

cc: ANDA: 76-500
DUP/DIVISION FILE
HFD-613/AVezza/LGolson (no cc)
aev/5/17/04|V:\FIRMSAM\BAXTER\LTRS&REV\76500.TAPL2
Review

(superseded by TA summary dated 5/19/04)

**TENTATIVE APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number: **76-500**

Date of Submission: **February 24, 2003**

Applicant's Name: **Baxter Healthcare Corporation**

Established Name: **Adenosine Injection USP, 3 mg/mL 2 mL single dose vials**

BASIS OF APPROVAL:

Patent Data – 19-937

No	Expiration	Use Code	Use	File
4673563	6-16-04		Adenosine in the treatment of supraventricular tachycardia	III

Exclusivity Data - 19-937

Code/sup	Expiration	Use Code	Description	Labeling Impact
None			There is no unexpired exclusivity for this product	

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? No – Tentative Approval

Container Labels: 2 mL

Satisfactory in FPL as of September 23, 2002 submission [v 1.1].

Carton Labeling: 10 x 2 mL

Satisfactory in FPL as of February 24, 2003 submission [v 2.1].

Professional Package Insert Labeling:

Satisfactory in draft as of February 24, 2003 submission [v 2.1].

Revisions needed post-approval: None

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Adenocard®

NDA Number: 19-937

NDA Drug Name: Adenocard® (adenosine injection)

NDA Firm: Fujisawa

Date of Approval of NDA Insert and supplement # 4-20-99 (S-015):

Has this been verified by the MIS system for the NDA? YES

Was this approval based upon an OGD labeling guidance? NO

Basis of Approval for the Container Labels:

Basis of Approval for the Carton Labeling:

Other Comments

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 25	X		

Is this name different than that used in the Orange Book?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? NO.		X	
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?		X	
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			X
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			X
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		X	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			X
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			X
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.	X		

NOTES TO THE CHEMIST:

- I have asked the firm to revise their storage temperature recommendations to read "Store at 20 - 25°C (68 - 77°F)[see USP Controlled Room Temperature]. Does the submitted stability data support these storage temperature recommendations?

2. Please note that the pH range listed for the RLD for this drug product is 5.5 to 7.5 while this ANDA has the same pH range as listed in the most current USP (4.5 to 7.5).
-
-

FOR THE RECORD: (portions taken from previous review)

1. Review based on the labeling of Adenocard®, revised 2-99; approved 4-20-99. This is NDA 19-937/S-015
 2. Patent/ Exclusivities

There is one patent - 4673563 - which expires 6-16-04. The firm has certified PIII to this patent. There are no exclusivities.
 3. Storage Conditions:
NDA - Store at controlled room temperature 15°-30°C (59°-86°F).
ANDA – [carton] - Store at 20°-25°C (68°-77°F)[See USP Controlled Room Temperature] – [insert] - Store at 20°-25°C (68°-77°F), excursions permitted to 15° -30°C (59° - 86°F). [See USP Controlled Room Temperature].
USP - Preserve in a single-dose container, preferably of Type I glass.
 4. Product Line:
The innovator markets their product in 10 x 2 mL vials and 5 x 2 mL and 5 x 4 mL disposable syringes
The applicant proposes to market their product in 10 x 2 mL vials (ANDA 76-500) and 5 x 2 mL syringes (ANDA 76-501)
 5. Inactive Ingredients:
The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing in section 4 (p 12, Volume 1.1).
 6. Baxter is the manufacturer (p 179 v 1.2 section 9).
 7. The vials are made of ~~one~~ Type 1 glass and they have green flip-off caps (p 487 v 1.4)..
 8. This ANDA shares an insert with ANDA 76-501 which is for the syringes. Both must be approved together or the insert has to be revised
-
-

Date of Review: 3-6-03

Date of Submission: 2-24-03

Primary Reviewer: Adolph Vezza

Date:

3/14/03

Team Leader: Lillie Golson

Date:

3/14/03

cc: ANDA: 76-500
DUP/DIVISION FILE
HFD-613/AVezza/LGolson (no cc)
aev/3/6/03|V:\FIRMSAM\BAXTER\LTRS&REV\76500.TAPL
Review

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 76-500

Date of Submission: September 23, 2002

Applicant's Name: Baxter Healthcare Corporation

Established Name: Adenosine Injection USP, 3 mg/mL 2 mL vials

Labeling Deficiencies:

1. GENERAL COMMENT

Revise your storage temperature recommendations throughout your labels and labeling as follows:

Store at 20 - 25°C (68 - 77°F)[see USP Controlled Room Temperature].

2. CARTON

See GENERAL COMMENT above.

3. INSERT

a. GENERAL COMMENT

We note that this ANDA shares an insert with your unapproved ANDA 76-501 for Adenosine Injection USP, 3 mg/mL 2 mL syringes. These ANDAs must be approved together or the insert labeling must be revised.

b. DESCRIPTION

We note that your drug product's pH range differs from that of the innovator ("4.5 and 7.5" vs "5.5 and 7.5"). Please comment and/or revise.

c. CLINICAL PHARMACOLOGY

i. Mechanism of Action, first line - Delete ~~_____~~

ii. Hemodynamics, first line - Delete ~~_____~~

d. WARNINGS

Bronchoconstriction, first line - Delete ~~_____~~

e. PRECAUTIONS

i. Drug Interactions

A). First line - Delete ~~_____~~

BASIS OF APPROVAL:

Patent Data – 19-937

No	Expiration	Use Code	Use	File
4673563	6-16-04		Adenosine in the treatment of supraventricular tachycardia	III

Exclusivity Data - 19-937

Code/sup	Expiration	Use Code	Description	Labeling Impact
None			There is no unexpired exclusivity for this product	

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

Do you have 12 Final Printed Labels and Labeling? Yes No If no, list why:

Container Labels: 2 mL

Carton Labeling: 10 x 2 mL

Professional Package Insert Labeling:

Revisions needed post-approval:

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Adenocard®

NDA Number: 19-937

NDA Drug Name: Adenocard® (adenosine injection)

NDA Firm: Fujisawa

Date of Approval of NDA Insert and supplement # 4-20-99 (S-015):

Has this been verified by the MIS system for the NDA? YES

Was this approval based upon an OGD labeling guidance? NO

Basis of Approval for the Container Labels:

Basis of Approval for the Carton Labeling:

Other Comments

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 25	X		
Is this name different than that used in the Orange Book?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? NO.		X	
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?		X	
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			

Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			X
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			X
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		X	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			X
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?			X
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.	X		

NOTE TO THE CHEMIST:

I have asked the firm to revise their storage temperature recommendations to read "Store at 20 - 25°C (68 - 77°F)[see USP Controlled Room Temperature]. Does the submitted stability data support these storage temperature recommendations?

FOR THE RECORD:

- Review based on the labeling of Adenocard®, revised 2-99; approved 4-20-99. This is NDA 19-937/S-015
- Patent/ Exclusivities
There is one patent - 4673563 - which expires 6-16-04. The firm has certified PIII to this patent. There are no exclusivities.
- Storage Conditions:
NDA - Store at controlled room temperature 15°-30°C (59°-86°F).
ANDA - Store at controlled room temperature 15° -30°C (59° - 86°F).
USP - Preserve in a single-dose container, preferably of Type I glass.

4. Product Line:
The innovator markets their product in 10 x 2 mL vials and 5 x 2 mL and 5 x 4 mL disposable syringes
The applicant proposes to market their product in 10 x 2 mL vials (ANDA 76-500) and 5 x 2 mL syringes (ANDA 76-501)
5. Inactive Ingredients:
The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing in section 4 (p 12, Volume 1.1) .
6. Baxter is the manufacturer (p 179 v 1.2 section 9).
7. The vials are made of — Type 1 glass and they have green flip-off caps (p 487 v 1.4)..
8. This ANDA shares an insert with ANDA 76-501 which is for the syringes. Both must be approved together or the insert has to be revised

Date of Review: 11-13-02

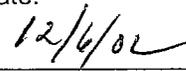
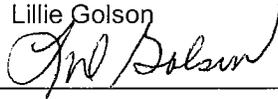
Date of Submission: 9-23-02

Primary Reviewer: Adolph Vezza

Date:

Team Leader: Lillie Golson

Date:



cc: ANDA: 76-500
DUP/DIVISION FILE
HFD-613/AVezza/LGolson (no cc)
aev/11/13/02|V:\FIRMSAM\BAXTER\LTRS&REV\76500na1.l
Review

**APPEARS THIS WAY
ON ORIGINAL**

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

76-500

CHEMISTRY REVIEW(S)

#1

✓ **ANDA 76-500**

**Adenosine Injection, USP
3 mg/mL in 2 mL Vials**

Baxter Healthcare Corporation

**Bitra Mirzai-Azarm
Division of Chemistry II**

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Chemistry Review Data Sheet

1. ANDA 76-500
2. REVIEW #: 1
3. REVIEW DATE: 21-JAN-2003
4. REVIEWER: Bita Mirzai-Azarm
5. PREVIOUS DOCUMENTS: N/A (Review #1)

Previous Documents

Document Date

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed

Document Date

Original

23-SEP-2002

7. NAME & ADDRESS OF APPLICANT:

Name: Baxter Healthcare Corporation, Anesthesia and
Critical Care.

Address: 95 Spring Street
New Providence, New Jersey 07974

Representative: Priya Jambhekar

Telephone: (908)286-7215



Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: N/A
b) Non-Proprietary Name (USAN): Adenosine Injection, USP

9. LEGAL BASIS FOR SUBMISSION:

Innovator Product: Adenocard
Innovator Company: Fugisawa Healthcare, Inc.
NDA Number: 19-937

10. PHARMACOL. CATEGORY:

Conversion to sinus rhythm of paroxysmal supraventricular tachycardia (PSVT)

11. DOSAGE FORM:

Injection

12. STRENGTH/POTENCY:

3 mg/mL, 2 mL single-dose vial

13. ROUTE OF ADMINISTRATION:

IV

14. Rx/OTC DISPENSED: Rx OTC15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product – Form Completed

Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Molecular Formula: $C_{10}H_{13}N_5O_4$

Molecular Weight: 267.24

17. RELATED/SUPPORTING DOCUMENTS:

APPEARS THIS WAY
ON ORIGINAL



CHEMISTRY REVIEW



Chemistry Review Data Sheet

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
---	II	---	---	1	Inadequate	01/21/03	
---	III	---	---	4			
---	III	---	---	4			
---	V	---	---				
---	III	---	---	4			

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Pending		
EES	Pending		
Methods Validation	USP Product		
Labeling	Not Approved	12/06/02	A. Veza
Bioequivalence	Pending		
EA			
Radiopharmaceutical			



CHEMISTRY REVIEW



Chemistry Review Data Sheet

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. Yes No If no, explain reason(s) below:

APPEARS THIS WAY
ON ORIGINAL

The Chemistry Review for ANDA 76-500

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application is Not Approvable – Minor

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug Product: Clear, colorless solution, essentially free from visible signs of contamination of any foreign material and particles, pH 4.5 – 7.5

The components are compounded in a _____ into flip-top type I glass vials, stoppered with _____ closures and _____

Drug Substance: White to off-white crystalline powder, soluble in water and practically insoluble in alcohol.

B. Description of How the Drug Product is Intended to be Used

The product should be given by rapid bolus IV only. It may be given via a IV line but should be followed by a rapid saline IV flush. No diluents are recommended in the package insert.

The product should not be refrigerated as crystallization may occur. If crystallization has occurred dissolve crystals by warming to room temperature. The solution must be clear at the time of use.

C. Basis for Approvability or Not-Approval Recommendation

This application is not approvable at this time. The NA Minor letter will be issued based on CMC issues. Bio, Micro and EER are pending.

Executive Summary Section

III. Administrative**A. Reviewer's Signature****B. Endorsements**

HFD-6 47/B.M.Azarm/01/21/03;1/27/03

HFD-647/U.Venkataram/1.24.03;1/27/03

HFD-617/S.Shepperson/1.27.03

C. CC: ANDA 76-500
 ANDA DUP
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ON ORIGINAL**

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✓ **ANDA 76-500**

**Adenosine Injection, USP
3 mg/mL in 2 mL Vials**

Baxter Healthcare Corporation

**Bitra Mirzai-Azarm
Division of Chemistry II**

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P DRUG PRODUCT [Name, Dosage form]	
A APPENDICES	
R REGIONAL INFORMATION.....	
II. Review Of Common Technical Document-Quality (Ctd-Q) Module 1	
A. Labeling & Package Insert.....	
B. Environmental Assessment Or Claim Of Categorical Exclusion.....	
III. List Of Deficiencies To Be Communicated.....	



A2

Chemistry Review Data Sheet

1. ANDA 76-500
2. REVIEW #: 2
3. REVIEW DATE: 18-APR-2003
4. REVIEWER: Bitu Mirzai-Azarm

5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
Original	23-SEP-2002

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Minor Amendment	24-FEB-2003
Microbiology amendment	09-APR-2003

7. NAME & ADDRESS OF APPLICANT:

Name: Baxter Healthcare Corporation, Anesthesia and
Critical Care.
Address: 95 Spring Street
New Providence, New Jersey 07974
Representative: Priya Jambhekar
Telephone: (908)286-7215



Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: N/A
b) Non-Proprietary Name (USAN): Adenosine Injection, USP

9. LEGAL BASIS FOR SUBMISSION:

Innovator Product: Adenocard
Innovator Company: Fugisawa Healthcare, Inc.
NDA Number: 19-937

10. PHARMACOL. CATEGORY:

Conversion to sinus rhythm of paroxysmal supraventricular tachycardia (PSVT)

11. DOSAGE FORM:

Injection

12. STRENGTH/POTENCY:

3 mg/mL, 2 mL single-dose vial

13. ROUTE OF ADMINISTRATION:

IV

14. Rx/OTC DISPENSED: Rx OTC15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product – Form Completed

Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Molecular Formula: $C_{10}H_{13}N_5O_4$

Molecular Weight: 267.24

**APPEARS THIS WAY
ON ORIGINAL**



CHEMISTRY REVIEW



Chemistry Review Data Sheet

**APPEARS THIS WAY
ON ORIGINAL**

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
_____	II	_____	_____	1	Adequate	04/17/03	
_____	III	_____	_____	4			
_____	III	_____	_____	4			
_____	V	_____	_____				
_____	III	_____	_____	4			

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

**APPEARS THIS WAY
ON ORIGINAL**



CHEMISTRY REVIEW



Chemistry Review Data Sheet

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Approved	16-APR-2003	Lisa Shelton
EES	Pending	12-NOV-2002	
Methods Validation	USP Product		
Labeling	Approved	14-MAR-2003	Adolph Vezza
Bioequivalence	Acceptable	31-JAN-2003	Lin-Whei Chuang
EA			
Radiopharmaceutical			

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ___ Yes No If no, explain reason(s) below:

Minor Amendment.

**APPEARS THIS WAY
ON ORIGINAL**

The Chemistry Review for ANDA 76-500

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application may be approved.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug Product: The drug product is Qualitatively and Quantitatively same as the RLD. Clear, colorless solution, essentially free from visible signs of contamination of any foreign material and particles, pH 4.5 – 7.5 (same pH range as listed in the most current USP).

The components are compounded in a _____ into flip-top type I glass vials, stoppered with _____

It is proposed to be marketed in 10x2 mL vials.

Drug Substance: White to off-white crystalline powder, soluble in water and practically insoluble in alcohol. Particle size and other physical characteristics have no bearing on the DP quality for this injectable drug. The drug substance is _____ (DMF _____). The DMF is satisfactory.

APPEARS THIS WAY
ON ORIGINAL

Executive Summary Section**B. Description of How the Drug Product is Intended to be Used**

The product should be given by rapid bolus IV only. It may be given via a IV line but should be followed by a rapid saline IV flush. No diluents are recommended in the package insert.

The product should not be refrigerated as crystallization may occur. If crystallization has occurred dissolve crystals by warming to room temperature. The solution must be clear at the time of use.

C. Basis for Approvability or Not-Approval Recommendation

The applicant has addressed all deficiencies. This application may be approved.

**APPEARS THIS WAY
ON ORIGINAL**



Executive Summary Section

III. Administrative

A. Reviewer's Signature

B. Endorsements

HFD-6 47/B.M.Azarm/04/21/03

Bita M. Azarm 04/28/03

HFD-647/U.Venkataram/4.23.03

HFD-617/S.Shepperson/4.23.03

C. CC: ANDA 76-500
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information

#3

ANDA 76-500

Adenosine Injection USP,

3 mg/mL in 2 mL Vials

Baxter Healthcare Corporation

**Bitra Mirzai-Azarm
Division of Chemistry II**



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 C. CC Block.....8

Chemistry Assessment ~~Error! Bookmark not defined.~~

I. Review Of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body Of Data.....

 S DRUG SUBSTANCE [Name, Manufacturer]

 P DRUG PRODUCT [Name, Dosage form].....

 A APPENDICES.....

 R REGIONAL INFORMATION.....

II. Review Of Common Technical Document-Quality (Ctd-Q) Module 1

 A. Labeling & Package Insert.....

 B. Environmental Assessment Or Claim Of Categorical Exclusion.....

III. List Of Deficiencies To Be Communicated.....



Chemistry Review Data Sheet

1. ANDA 76-500
2. REVIEW #: 3
3. REVIEW DATE: 01-JUN-2004
4. REVIEWER: Bita Mirzai-Azarm

5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
Original	23-SEP-2002
Minor Amendment	24-FEB-2003
Microbiology amendment	09-APR-2003

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Minor Amendment (Request for Final approval)	28-APR-2004
Labeling Amendment	25-MAY-2004

7. NAME & ADDRESS OF APPLICANT:

Name: Baxter Healthcare Corporation, Anesthesia and
Critical Care.
Address: 95 Spring Street
New Providence, New Jersey 07974
Representative: Ivy Bautista
Telephone: (908)286-7393



Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: N/A
- b) Non-Proprietary Name (USAN): Adenosine Injection, USP

9. LEGAL BASIS FOR SUBMISSION:

Innovator Product: Adenocard
Innovator Company: Fugisawa Healthcare, Inc.
NDA Number: 19-937

10. PHARMACOL. CATEGORY:

Conversion to sinus rhythm of paroxysmal supraventricular tachycardia (PSVT)

11. DOSAGE FORM:

Injection

12. STRENGTH/POTENCY:

3 mg/mL, 2 mL single-dose vial

13. ROUTE OF ADMINISTRATION:

IV

14. Rx/OTC DISPENSED: Rx OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product – Form Completed

Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Molecular Formula: $C_{10}H_{13}N_5O_4$

Molecular Weight: 267.24

17. RELATED/SUPPORTING DOCUMENTS:

APPEARS THIS WAY
ON ORIGINAL



CHEMISTRY REVIEW



Chemistry Review Data Sheet

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
	II			1	Adequate	04/17/03	
	III			4			
	III			4			
	V						
	III			4			

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 – Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Approved	16-APR-2003	Lisa Shelton
EES	Acceptable	15-MAY-2003	
Methods Validation	USP Product		
Labeling	Approved	08-JUN-2004	Adolph Vezza
Bioequivalence	Acceptable	31-JAN-2003	Lin-Whei Chuang
EA			
Radiopharmaceutical			



CHEMISTRY REVIEW



Chemistry Review Data Sheet

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ___ Yes ___ X No If no, explain reason(s) below:

Minor Amendment.

**APPEARS THIS WAY
ON ORIGINAL**



The Chemistry Review for ANDA 76-500

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Recommended for FINAL approval. See remarks.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug Product: The drug product is Qualitatively and Quantitatively same as the RLD. Clear, colorless solution, essentially free from visible signs of contamination of any foreign material and particles, pH 4.5 – 7.5 (same pH range as listed in the most current USP).

The components are compounded in a _____ into flip-top type I glass vials, stoppered with _____

_____ . It is proposed to be marketed in 10x2 mL vials.

Drug Substance: White to off-white crystalline powder, soluble in water and practically insoluble in alcohol. Particle size and other physical characteristics have no bearing on the DP quality for this injectable drug. The drug substance is _____ DMF
The DMF is satisfactory.



Chemistry Assessment Section

B. Description of How the Drug Product is Intended to be Used

The product should be given by rapid bolus IV only. It may be given via a IV line but should be followed by a rapid saline IV flush. No diluents are recommended in the package insert.

The product should not be refrigerated as crystallization may occur. If crystallization has occurred dissolve crystals by warming to room temperature. The solution must be clear at the time of use.

C. Basis for Approvability or Not-Approval Recommendation

The ANDA was tentatively approved on May 14, 2003. The applicant submitted a minor amendment on April 28, 2004 to request for FINAL approval. The applicant submitted 18 months stability data for the drug product. Results are within specifications. The applicant also reported the addition of an alternate stability testing site for the DP. This site is already listed in the ANDA as a release testing site for the DP.

Baxter Pharmaceutical Solutions LLC
927 S. Curry Pike, PO Box 3068
Bloomington, Indiana 47402

In addition, the applicant reported change in the color of the stopper seal from green to white. This part of stopper has no direct contact with the DP.

Recommended for FINAL approval.

III. Administrative

A. Reviewer's Signature

B. Endorsements

HFD-6 47/B.M.Azarm/6/1/04

B.M. Azarm 6/14/04.

HFD-647/U.Venkataram/6.1.04

U.V. Venkataram 6/14/04.

HFD-617/S.Shepperson/6-10-04

S. Shepperson 6/14/04

CC list:

ANDA 76-500

ANDA DUP

DIV FILE

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CHEMISTRY REVIEW



Chemistry Assessment Section

F/T by sms 6-10-04

V:\FIRMSAM\BAXTER\LTRS&REV\76500N03.RBM

TYPE OF LETTER: FINAL APPROVABLE

**APPEARS THIS WAY
ON ORIGINAL**

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**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

76-500

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review

Review for HFD-640

April 16, 2003

ANDA: 76-500

Drug Product Name

Proprietary: N/A

Non-proprietary: Adenosine Injection, USP

Drug Product Classification: N/A

Review Number: #1

Subject of this Review

Submission Date: September 23, 2002 (Original) and April 9, 2003
(Telephone Amendment)

Receipt Date: September 24, 2002 (Original) and April 10 (Telephone
Amendment)

Consult Date: N/A

Date Assigned for Review: March 11, 2003

Submission History (for amendments only)

Date(s) of Previous Submission(s): N/A

Date(s) of Previous Micro Review(s): N/A

Applicant/Sponsor

Name: Baxter Healthcare Corporation, Anesthesia and Critical Care

Address: 95 Spring Street, New Providence, NJ 7974

Representative: Priya Jambhekar

Telephone: 908-286-7215

Name of Reviewer: Lisa S.G. Shelton

Conclusion: The submission is **recommended for approval on the basis of sterility assurance.**

Product Quality Microbiology Data Sheet

- A.**
1. **TYPE OF SUPPLEMENT:** N/A
 2. **SUPPLEMENT PROVIDES FOR:** N/A
 3. **MANUFACTURING SITE:**
 Baxter Pharmaceutical Solutions, LLC
 927 S. Curry Pike
 Bloomington, IN 47402
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile injection, IV, packaged as 3 mg/mL (6 mg/2 mL) in a 2 mL single dose vial
 5. **METHOD(S) OF STERILIZATION:** ~~_____~~
 6. **PHARMACOLOGICAL CATEGORY:** Anti-arrhythmics

B. SUPPORTING/RELATED DOCUMENTS:

- DMF ~~_____~~ (Type II) - ~~_____~~
- DMF ~~_____~~ - USP 1 Glass Vial - ~~_____~~
- DMF ~~_____~~ Stopper - ~~_____~~
- DMF ~~_____~~ (Type V) - ~~_____~~
- DMF ~~_____~~ (Type III) - ~~_____~~

C. REMARKS:

ANDAs 76-500 and 76-501 include drug products that are identical except for the container/closure system, 2 mL vial and 2 mL syringe, respectively. Clarifying questions discussed by telephone (4/4/03), regarding the inclusion of BI in the annual requalification and the ~~_____~~ suspension count used for BIs, are addressed in a Telephone Amendment, dated 4/9/03.

filename: V:\MICROREV\76-500.doc

Executive Summary

I. Recommendations

- A. Recommendation on Approvability –**
The submission is **recommended** for approval on the basis of sterility assurance. Specific comments are provided in the "Product Quality Microbiology Assessment" section.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A**

II. Summary of Microbiology Assessments

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology –** Stopped vials are _____ using a _____ processing for bioburden reduction is performed. The subject drug product is _____ filled into pre-sterilized vials. Glass vials are _____ . Stoppers are _____
- B. Brief Description of Microbiology Deficiencies – N/A**
- C. Assessment of Risk Due to Microbiology Deficiencies –**
The safety risk is considered minimal.

III. Administrative

- A. Reviewer's Signature** *Lisa S.G. Shelton*
- B. Endorsement Block**
Microbiologist, Lisa S.G. Shelton, Ph.D. *lgs 4/16/03*
Microbiology Team Leader, Neal J. Sweeney, Ph.D.
- C. CC Block**
cc:
Original ANDA 76-500
Division File
Field Copy

Neal J. Sweeney 4/17/03

Redacted 9

Page(s) of trade

secret and /or

confidential

commercial

information

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

76-500

**BIOEQUIVALENCE
REVIEW(S)**

**OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE**

AND A # 76-500 & 76-501

APPLICANT: Baxter Healthcare Corporation, Anesthesia & Critical Care.

DRUG PRODUCT: Adenosine Injection, USP, 3 mg/mL,
in 2 mL single-dose vials and
in 2 mL single-dose syringes

TYPES OF STUDIES: Waiver Request

RESULTS: Waiver granted per 21 CFR Section 320.22(b)(1)

PRIMARY REVIEWER : Lin-Whei Chuang BRANCH : I

INITIAL : LWC DATE : 1/17/03

BRANCH CHIEF : Yih-Chain Huang, Ph.D. BRANCH : I

INITIAL : YCH DATE : 1/17/2003

DIRECTOR
DIVISION OF BIOEQUIVALENCE : Dale P. Conner, Pharm.D.

INITIAL : DPC DATE : 1/31/03

**APPEARS THIS WAY
ON ORIGINAL**

JAN 31 2003

Adenosine Injection, USP

3 mg/mL,

2 mL Single-Dose vial

ANDA #76-500

2 mL Single-Dose Syringe

ANDA #76-501

Reviewer: Lin-Whei Chuang

V:\FIRMSAM\BAXTER\LTRS&REV\76500W0902.doc

Baxter Healthcare Corp.

Anesthesia and Critical Care

New Providence, NJ

Submission Date:

September 23, 2002

Review of a Waiver Request

These two ANDAs are based on Adenocard® IV (adenosine injection, available as 2 mL vials, 2 mL syringes, and 4 mL syringes) for rapid bolus intravenous. Adenocard® was approved through NDA #19937 on 5/18/1995 for Fujisawa Healthcare, Inc.. The therapeutic effect of adenosine is based on its antiarrhythmic activity.

The firm is requesting a waiver of in vivo BE requirements for the test drug per 21 CFR 320.22 (b) (1).

Formulation Comparison

Ingredient	Test Drug (Baxter)	Reference* (Fujisawa)
Adenosine	3 mg/mL	3 mg/mL
Sodium Chloride, USP	9 mg/mL	9 mg/mL
Water for Injection, USP	q.s.	q.s.

* = From COMIS

Comments:

1. The drug product is a parental solution intended solely for administration by injection.
2. The test drug product contains the same active and inactive ingredients in the same concentration as Adenocard® IV.
3. The waiver of in vivo bioequivalence study requirements can be granted based on 21 CFR section 320.22(b) (1) of the Bioavailability/Bioequivalence Regulations.

APPEARS THIS WAY
ON ORIGINAL

RECOMMENDATION

The Division of Bioequivalence agrees that the information submitted by Baxter Healthcare Corporation demonstrates that its adenosine injection, USP, 3 mg/mL in 2 mL vials and in 2 mL syringes, fall under 21 CFR Section 320.22(b)(1) of Bioavailability/Bioequivalence Regulations. The waiver of *in vivo* bioequivalence requirements for adenosine Injection, USP, 3 mg/mL in 2 mL vials and 2 mL syringes of the test product is granted. From the bioequivalence point of view, the Division of Bioequivalence deems Baxter's adenosine Injection, USP, 3 mg/mL in 2 mL vials and in 2 ml syringes bioequivalent to the reference listed drug, Fujisawa's Adenocard® IV (adenosine injection), 3 mg/mL.

Lin-Whei Chuang 1/17/03

Lin-Whei Chuang
Division of Bioequivalence
Review Branch I

RD INITIALLED YHUANG
FT INITIALLED YHUANG

[Signature] Date 1/17/2003

Concur *[Signature]* Date: 1/3/03

for Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence

**APPEARS THIS WAY
ON ORIGINAL**

BIOEQUIVALENCY COMMENTS

ANDA: #76-500 &
#76-501

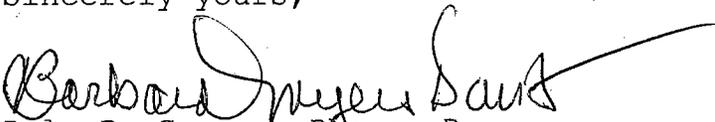
APPLICANT: Baxter Healthcare Corporation, Anesthesia &
Critical Care.

DRUG PRODUCT: Adenosine Injection USP, 3 mg/mL,
in 2 mL single-dose vials and
in 2 mL single-dose syringes

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

for 
Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

**APPEARS THIS WAY
ON ORIGINAL**

CC: ANDA #76-500 & 76-501
ANDA DUPLICATE
DIVISION FILE
HFD-652/ Bio Secretary - Bio Drug File
HFD-652/ Lin-Whei Chuang

Endorsements: (Final with Dates)
HFD-652/ L. Chuang *ZWC 1/17/03*
HFD-652/ Y. Huang *YH 1/17/2003*
HFD-617 A. Sigler *AS 1/17/2003*
der HFD-650/ D. Conner *DC 1/31/03*

V:\FIRMSAM\BAXTER\LTRS&REV\76500W0902.doc

BIOEQUIVALENCY - ACCEPTABLE

WAIVER (WAI) *OK*

Strength: 3mg/mL
Outcome: AC

Outcome Decisions: Acceptable
AC - Acceptable

WINBIO COMMENTS: The waiver is granted

**APPEARS THIS WAY
ON ORIGINAL**

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

76-500

**ADMINISTRATIVE
DOCUMENTS**

Redacted _____

*T-Can
Manufacturing
process*

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information

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

76-500

CORRESPONDENCE

BaxterVia Fed Ex Overnight Express

May 25, 2004

ORIG AMENDMENT

N/AF

Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room - MPN-2
7500 Standish Place, Room 150
Rockville, MD 20855-2773Attention: Mr. Gary Buehler, Director, Office of Generic Drugs [OGD], HFD-600
Desk copy: Mr. Adolph Vezza, Director, RegulatoryRe: **ANDA 76-500 - Adenosine Injection, USP, 3 mg/mL in 2 mL Vials**
Final Package Labels

Dear Mr. Buehler:

Reference is made to Baxter Healthcare Corporation, Anesthesia and Critical Care abbreviated new drug application (ANDA) 76-500, for Adenosine Injection USP, 3 mg/mL packaged in 2 mL single-dose vials submitted on September 23, 2002.

Reference is also made to the Agency's letter dated May 14, 2003 granting a tentative approval for the ANDA.

Reference is also made to telephone conversation on May 18, 2004, between FDA (Mr. Adolph Vezza) and the undersigned where final package labels (FPL) for the package insert and the container label were requested for the final approval of the ANDA.

Enclosed as an Attachment are twelve (12) copies of the FPL for the container and the package insert.

Should you have any questions, please do not hesitate to contact me at 908/286-7393, or by facsimile at 908/286-7269.

Sincerely,


Ivy Bautista
Assoc. Director, Regulatory Affairs**RECEIVED**

MAY 26 2004

OGD/CDER

Baxter
Via Airborne Overnight Express

*Labeling review EER &
drafted 5/12/04
A. Vezza*

SS 5/17/04

ORIG AMENDMENT

AM

April 28, 2004

Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room - MPN-2
7500 Standish Place, Room 150
Rockville MD 20855-2773

Attention: Mr. Gary Buehler, Director, Office of Generic Drugs [OGD], HFD-600
Desk copy: Dr. Stanley Shepperson, Project Manager

re: **ANDA 76-500 - Adenosine Injection, USP, 3 mg/mL in 2 mL Vials**
MINOR AMENDMENT: FINAL APPROVAL REQUESTED

Dear Mr. Buehler:

Reference is made to Baxter Healthcare Corporation, Anesthesia and Critical Care abbreviated new drug application (ANDA) 76-500, for Adenosine Injection USP, 3 mg/mL packaged in 6 mg/2 mL single-dose vials submitted on September 23, 2002.

Reference is also made to the Agency's letter dated May 14, 2003 granting a tentative approval for the ANDA.

Baxter Healthcare Corporation, Anesthesia & Critical Care [Baxter Healthcare, A&CC] is amending the ANDA to request for the final approval of the Application after the '563 patent for Adenocard® Injection expires on June 16, 2004.

Baxter Healthcare, A&CC believes that the ANDA is eligible for final approval because the product is still in the same condition as when it was tentatively approved with the following are updates to the ANDA:

- Stability data for the drug product after 18 months of storage (Attachment 1)
- Package insert editing revisions- enclosed as Attachment 2 is the version that was last submitted into the ANDA (February 2003), the marked-up revised version and the revised version of the package insert.

APR 29 2004
CLAUDE

Mr. Gary Buehler
February 24, 2003
Page 2

- Addition of an alternate stability testing site. This site is already listed in the ANDA as a release testing site for the drug product.

Baxter Pharmaceutical Solutions LLC
927 S. Curry Pike, PO Box 3068
Bloomington, Indiana 47402
(812) 333-0887
Drug Establishment No.: 1833527

The last FDA inspection of this facility was on July 2002. There are no outstanding FDA 483s.

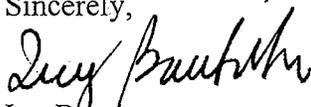
- Change in the color of the stopper seal from green to white. This part of the stopper has no direct contact with the drug product.

If the addition of an alternate testing facility and the change in the color of the stopper seal will impact on the timelines for Final Approval of the ANDA, Baxter will file these changes as a post approval supplement.

Please note that Baxter Healthcare, A&CC, is submitting the same request for final approval under separate cover to ANDA 76-501 for Adenosine Injection, USP packaged in 2 mL syringes.

Should you have any questions, please do not hesitate to contact at 908/286-7393, or by facsimile at 908/286-7269.

Sincerely,



Ivy Bautista
Assoc. Director, Regulatory Affairs

Baxter

April 9, 2003

via Facsimile and Airborne Overnight ExpressORIG AMENDMENT
NIASFood and Drug Administration
Center for Drug Evaluation and Research
Document Control Room - MPN-2
7500 Standish Place, Room 150
Rockville MD 20855-2773Attention: Mr. Gary Buehler, Director, Office of Generic Drugs [OGD], HFD-600
Desk copies: Mr. Stanley Shepperson, Project Manager
Ms. Lisa Shelton, Microbiology Reviewerre: **ANDA 76-500 - Adenosine Injection, USP, 3 mg/mL in 2 mL Vials**
TELEPHONE AMENDMENT: *Submission of Microbiological Information*

Dear Mr. Buehler:

Reference is made to the above-mentioned pending application for ANDA 76-500 - Adenosine Injection, 3 mg/mL, in 2 mL Vials, submitted on September 23, 2003. Reference is also made to a telephone conversation on April 4, 2003, between Baxter Healthcare Corporation, Anesthesia & Critical Care [Baxter Healthcare, A&CC] and Ms. Lisa Shelton, FDA-OGD Microbiology Reviewer, who requested clarification of selected information submitted in the Microbiology section of the ANDA. The following responses were provided verbally to the Agency during a telephone conversation with Ms. Shelton on April 7, 2003:

Question 1: Does the _____ study, which is carried out to achieve annual re-qualification of the _____ involve the use of Biological Indicators?

Answer: Yes

Question 2: The report entitled *Summary of the Performance Qualification for the Maximum and Minimum Qualification Load Configuration for the 2mL/13mm Vial* _____ (Attachment II, page 432) includes two different _____ populations of Biological Indicators [BIs] for Lot AR247. On pages 433 and 436, the value is stated as _____, and on pages 448 and 407 it is stated as _____. Please clarify.

Answer: Pages 448 and 407 include a _____ manufacturer's Certificate of Performance for Lot Number AR247 used in the load qualification study.

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APR 10 2003

OGD / CDER

Mr. Gary Buehler, HFD-600

April 9, 2003

Page 2

The _____ count for Lot AR263 is _____, which represents the population of _____ stock suspension in _____. The lower concentrations listed on pages 433 and 436 represent a _____ of _____ made by performing a _____ of the vendor-supplied stock suspension. After the _____ dilution is made, the BIs are made by transferring _____ yielding a BI with a _____ population of _____ which is then used for validation of the _____ process..

Please note that Baxter Healthcare, A&CC, is submitting under separate cover a similar Telephone Amendment to ANDA 76-501 for Adenosine Injection, USP packaged in 2 mL syringes.

The Field Copy, as per 21 CFR 314.96(b), is being submitted concurrently to the North Brunswick Resident Inspection Post of the Newark District Office.

Should you have any questions, please do not hesitate to contact Lidia Mostovy, by telephone at 908/286-7393, or me at 908/386-7215, or by facsimile at 908/286-7269, or by eMail to priya_jambhekar@baxter.com.

Sincerely,



Priya Jambhekar
Director, Regulatory Affairs

enc: Form FDA 356h

Baxter

February 24, 2003

*Labeling review
drafted 3/6/03
A. Vezze*

Via Airborne Overnight Express

Food and Drug Administration
Center for Drug Evaluation and Research
Document Control Room - MPN-2
7500 Standish Place, Room 150
Rockville MD 20855-2773

ORIG AMENDMENT
N/AM

Attention: Mr. Gary Buehler, Director, Office of Generic Drugs [OGD], HFD-600
Desk copy: Mr. Stanley Shepperson, Project Manager

re: **ANDA 76-500 - Adenosine Injection, USP, 3 mg/mL in 2 mL Vials**
MINOR AMENDMENT: *Response to faxed minor deficiency of February 3, 2003*

Dear Mr. Buehler:

Baxter Healthcare Corporation, Anesthesia & Critical Care [Baxter Healthcare, A&CC] herewith submits a full response to the faxed 2/3/03 minor deficiency letter (copy enclosed) received on ANDA 76-500, Adenosine Injection USP, 3 mg/mL packaged in 2 mL vials.

Section 1 includes responses to the Chemistry, Manufacturing, and Controls comments, and Section 2 includes responses to the Labeling comments. The Agency comments are listed in each section, in bold, in the order presented in the deficiency letter, followed by the Baxter Healthcare, A&CC responses. The Labeling section includes 12 sets of the final printed carton labels in the Archival copy, and 4 sets of *draft* package insert labeling in the Archival copy. This section also includes a side-by-side comparison between the current package insert, 460-360-01, and the September 2002, 460-360-00, version submitted with the original ANDA on 9/23/02. The Review and Field copies contain no labeling.

Details are as follows:

	Item	Page #
Section 1	CMC Responses	0001
Tab 1	Quantitative data	0003
Tab 2	USP <381> testing results	0009
Tab 3	Updated stability report	0017

*7/24
5/3/03*

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FEB 26 2003

OGD / CDER

Mr. Gary Buehler
February 24, 2003
Page 2

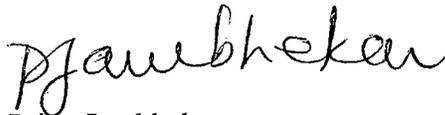
	Item	Page #
Section 2	Labeling Responses	0035
	Vials carton (12 sets, FPL)	0038
	Revised <i>draft</i> Package Insert (4 sets)	0050
	Package Insert comparisons	0086

The Field Copy (without the Labeling section), as per 21 CFR 314.96(b), is being submitted concurrently to the North Brunswick Resident Inspection Post of the Newark District Office.

Please note that Baxter Healthcare, A&CC, is submitting under separate cover a full response to the 2/7/03 faxed minor deficiency letter on ANDA 76-501 for Adenosine Injection, USP packaged in 2 mL syringes.

Should you have any questions, please do not hesitate to contact Lidia Mostovy at 908/286-7393, or me, by telephone at 908/386-7215, or by facsimile at 908/286-7269, or by eMail at priya_jambhekar@baxter.com.

Sincerely,



Priya Jambhekar
Director, Regulatory Affairs

enc: Form FDA 356h

ANDA 76-500

OCT 30 2002

Baxter Healthcare Corporation
Anesthesia & Critical Care
Attention: Priya Jambhekar
95 Spring Street
New Providence, NJ 07974

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Adenosine Injection USP, 3 mg/mL, 2 mL vials

DATE OF APPLICATION: September 23, 2002

DATE (RECEIVED) ACCEPTABLE FOR FILING: September 24, 2002

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Stanley Shepperson
Project Manager
(301) 827-5849

Sincerely yours,



Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Baxter

September 23, 2002

Via DC Express – Same Day DeliveryFood and Drug Administration
Center for Drug Evaluation and Research
Document Control Room - MPN-2
7500 Standish Place, Room 150
Rockville MD 20855-2773Attention: Mr. Gary Buehler
Director, Office of Generic Drugs [OGD]re: **Original ANDA - Adenosine Injection, USP;
3 mg/mL in 2 mL Vials**

Dear Mr. Buehler:

According to 21 CFR 314.94, Baxter Healthcare Corporation, Anesthesia & Critical Care (BHC, A&CC) is submitting in duplicate an ANDA for Adenosine Injection, USP (adenosine). Similar to the listed drug, Adenocard® (Adenosine Injection), this ANDA contains the adenosine 3 mg/mL in 2 mL Vials (6 mg total).

This submission is formatted in accordance with "Guidance for Industry: Organization of an Abbreviated New Drug Application and Abbreviated Antibiotic Application" (FDA/CDER, April 1997), and the ANDA sections are organized as follows:

ANDA Sections	Submission Volume
Cover Letter, Field Copy Documentation, Table of Contents.	1
1 – 8	1
9 – 12.2	2
12.3 <i>Sterility Assurance</i>	3
13 – 15	4
16 – 21	5
6 <i>Bio-equivalence review copy</i>	6
16 <i>Two extra sets of MVP</i>	7 & 8

RECEIVED

SEP 24 2002

OGD / CDER

*Labeling review
drafted 11/13/02
A. Vega*

*505(j)(2)(A) OK
30 OCT 2002
Gregory J. Davis*

Mr. Gary Buehler
September 23, 2002
Page 2

The archival copy is submitted in blue jackets, the Chemistry, Manufacturing, and Controls review copy is bound in red, and the Bio-equivalence review copy (volume 6) is in an orange jacket. Four (4) sets of *draft* labeling are included in the archival copy (Section 5) and two extra sets of the Methods Validation Package, volumes 7 and 8, are also included bound in black ACCO binders.

The Field Copy (volumes 1 through 6, without Section 5 - Labeling), as per 21 CFR 314.96(b), is being submitted concurrently to the North Brunswick Resident Inspection Post of the Newark District Office. Should you have any questions, please do not hesitate to contact me by telephone at 908/386-7215, or by facsimile at 908/286-7269.

Sincerely,



Priya Jambhekar
Director, Regulatory Affairs

enc: Form 356h; original ANDA