



NDA 20-920/S-003

Scios Inc.  
Attention: Ms. Jane A. Moffitt  
Vice President, Regulatory Affairs  
6500 Paseo Padre Parkway  
Fremont, CA 94555-3658

Dear Ms. Moffitt:

Please refer to your supplemental new drug application dated January 23, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Natrecor (nesiritide) for Injection.

This "Changes Being Effected" supplemental new drug application provides for final printed labeling revised as follows:

1. Throughout the labeling, "µg" has been replaced with "mcg."
2. Under **Clinical Trials**, the reference to the "ADVERSE REACTION section" in the first paragraph has been changed to "ADVERSE REACTIONS section."
3. The title of the **Effects of Symptoms** section has been changed to **Effects on Symptoms**.
4. Under **DOSAGE AND ADMINISTRATION**, the following text has been added at three different locations (under the main **DOSAGE AND ADMINISTRATION** heading, under the **Preparation** subheading, and under the **Dosing Instructions** subheading):

**The Natrecor bolus must be drawn from the prepared infusion bag.**

5. Under **DOSAGE AND ADMINISTRATION/Preparation**, bolded type is now used for "**Withdraw the entire contents of the reconstituted Natrecor vial.**"
6. Under **DOSAGE AND ADMINISTRATION**, the **Dosing Instructions** subsection has been substantially revised and now reads as follows:

**Dosing Instructions**

**The Natrecor bolus must be drawn from the prepared infusion bag.**

The recommended dose of Natrecor is an IV bolus of 2 mcg/kg followed by a continuous infusion of 0.01 mcg/kg/min. Natrecor should not be initiated at a dose that is above the recommended dose.

Prime the IV tubing with an infusion of 25 mL prior to connecting to the patient's vascular access port and prior to administering the bolus or starting the infusion.

The administration of the recommended dose of Natrecor is a two step process:

## Step 1. Administration of the IV Bolus

**After preparation of the infusion bag**, as described previously, withdraw the bolus volume (see Weight-Adjusted Bolus Volume table) from the Natrecor infusion bag, and administer it over approximately 60 seconds through an IV port in the tubing.

$$\text{Bolus Volume (mL)} = \text{Patient Weight (kg)} / 3$$

**Natrecor Weight-Adjusted Bolus Volume Administered Over 60 Seconds  
(Final Concentration = 6 mcg/mL)**

Patient Weight (kg)	Volume of Bolus (mL = kg/3)
60	20.0
70	23.3
80	26.7
90	30.0
100	33.3
110	36.7

## Step 2. Administration of the Continuous Infusion

Immediately following the administration of the bolus, infuse Natrecor at a flow rate of 0.1 mL/kg/hr. This will deliver a Natrecor infusion dose of 0.01 mcg/kg/min.

To calculate the infusion flow rate to deliver a 0.01 mcg/kg/min dose, use the following formula (see the following Weight-Adjusted Infusion Flow Rate for Dosing table):

$$\text{Infusion Flow Rate (mL/hr)} = \text{Patient Weight (kg)} \times 0.1$$

**Natrecor Weight-Adjusted Infusion Flow Rate for a 0.01 mcg/kg/min Dose following Bolus  
(Final Concentration = 6 mcg/ml)**

Patient Weight (kg)	Rate of Infusion (mL/hr)
60	6
70	7
80	8
90	9
100	10
110	11

7. The distribution address has been changed to:

6500 Paseo Padre Parkway  
Fremont, CA 94555

8. The copyright date has been changed to 2003.  
9. The control number has been changed from NA1030.02 to 20030300.  
10. The revision date has been changed to September 2003.

The carton labels have been revised as follows:

1. The Scios address has been changed to:

6500 Paseo Padre Pkwy  
Fremont, CA 94555

2. The directions for reconstitution have been changed from:

To reconstitute, add 5 mL of diluent (see package insert) into vial.

To:

**Natreacor must be diluted prior to infusion.** To reconstitute, add 5 mL of diluent (see package insert) into vial. After reconstitution, each mL contains 0.32 mg of nesiritide.

The container labels have been revised as follows:

1. The Scios address has been changed to Fremont, CA 94555.
2. The following text has been added:

**Natreacor must be diluted prior to infusion.** Each mL after reconstitution with 5 mL of diluent contains 0.32 mg of nesiritide.

We have completed our review of this supplemental new drug application. It is approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on January 23, 2004.

If you issue a letter communicating important information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410  
FDA  
5600 Fishers Lane  
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Mr. Russell Fortney  
Regulatory Health Project Manager  
(301) 594-5311

Sincerely,

*{See appended electronic signature page}*

Norman Stockbridge, M.D., Ph.D.  
Acting Director  
Division of Cardio-Renal Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research



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/s/

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Norman Stockbridge  
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