



NDA 20-920/S-008

Scios Inc.
Attention: Hana B. Moran, Ph.D.
Sr. Director, Regulatory Affairs
6500 Paseo Padre Parkway
Fremont, CA 94555-3658

Dear Dr. Moran:

Please refer to your supplemental new drug application dated April 18, 2005, 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 labeling to be revised as follows:

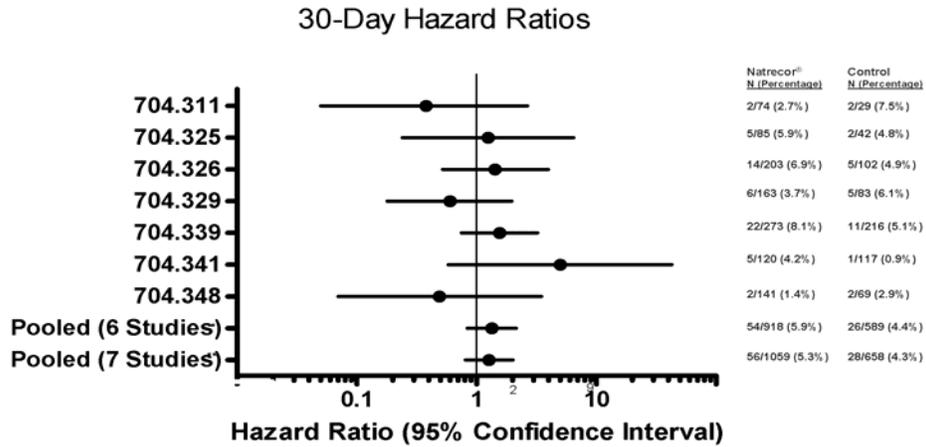
1. The **ADVERSE REACTIONS/Effect on Mortality** section has been changed from:

In the VMAC trial, the mortality rates at six months in the patients receiving Natrecor and nitroglycerin were 25.1% (95% confidence interval, 20.0% to 30.5%) and 20.8% (95% confidence interval, 15.5% to 26.5%), respectively. In all controlled trials combined, the mortality rates for Natrecor and active control (including nitroglycerin, dobutamine, nitroprusside, milrinone, amrinone, and dopamine) patients were 21.7% and 21.5%, respectively.

To:

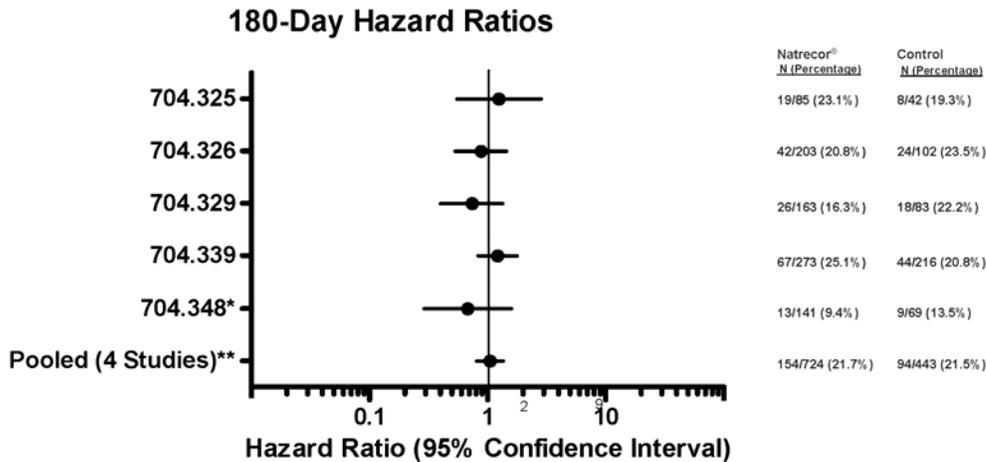
Data from all seven studies in which 30-day data were collected are presented in the chart below. The data depict hazard ratios and confidence intervals of mortality data for randomized and treated patients with Natrecor relative to active controls through day 30 for each of the 7 individual studies (Studies 311, 325, 326, 329 [PRECEDENT], 339 [VMAC], 341 [PROACTION], and 348 [FUSION I]).

The figure (on logarithmic scale) also contains a plot for the six studies involving hospitalized or Emergency Department patients combined (n = 1507), and for all 7 studies combined (n = 1717). The percentage is the Kaplan-Meier estimate.



* Studies 704.311, 704.325, 704.326, 704.329, 704.339, and 704.341
 ** Studies 704.311, 704.325, 704.326, 704.329, 704.339, 704.341, and 704.348

The figure below represents 180-day mortality hazard ratios for randomized and treated patients from all four individual studies where 180-day data were collected, 16 week hazard ratios for Study 348 (180-day data were not collected), and the four studies with 180-day data pooled (n = 1167).



* Data collected through week 16
 ** Studies 704.325, 704.326, 704.329, and 704.339

There were few deaths in these studies, so the confidence limits around the hazard ratios for mortality are wide. The studies are also small, so some potentially important baseline imbalances exist among the treatment groups, the effects of which cannot be ascertained.

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 agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling.

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, call 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

Enclosure

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Norman Stockbridge
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