Medicare May Halt Off-Label Nesiritide Coverage

The drug's use for the treatment of chronic heart failure called 'more risky' than previously thought.

BY DEEANNA FRANKLIN
Associate Editor

WASHINGTON — The Centers for Medicare and Medicaid Services may issue a national coverage determination that would deny coverage of nesiritide (Natrecor) for the treatment of chronic heart failure in Medicare beneficiaries.

Nesiritide is indicated only for the intravenous treatment of acute decompensated heart failure (ADHF) in hospitalized patients with dyspnea at rest or with minimal activity, such as talking, eating, or bathing. The CMS proposal would change only one aspect of existing coverage of the drug, specifically its off-label use in patients with chronic heart failure.

"We're keeping it for the [Food and Drug Administration] approved [indication] and for all the other off-label uses. It's just this one thing that seems more risky than we thought," said Don McLeod of the CMS press office. The agency will weigh public comments as well as other evidence before issuing a final determination.

According to Mark Wolfe, a spokesperson with Scios Inc.'s parent company, Johnson & Johnson, "The proposed national coverage determination is consistent with our own recommended use of Natrecor. Scios has ongoing studies involving Natrecor and will be keeping the [CMS] informed regarding this research."

In an October letter sent to health care providers, Scios emphasized that nesiritide "is safe and effective" when used for its current indication. It rebutted recent reports that suggested nesiritide adversely affected renal function and short-term mortality more than other drugs for ADHF. "These reports have included inaccurate information and selective analysis of data previously included in the prescribing information," stated the letter's author, Dr. Darlene Horton, senior vice president at Scios.

However, Dr. Jonathan Sackner-Bernstein, a prominent New York cardiologist and coauthor of several metaanalyses critical of nesiritide (N. Engl. J. Med. 2005;353:1525-7, JAMA 2005;293:1900-5) is unflinching in his contention that nesiritide "should be withdrawn from the market."

"No analysis by anyone in any context can be used to support the statement that nesiritide is shown to be safe. Therefore, according to the law, it should not be legal to sell it," Dr. Sackner-Bernstein said.

Many of his colleagues remain unconvinced that nesiritide should be withdrawn or that CMS' current action portends the drug's future withdrawal. "The FDA approval was for the treatment of decompensated heart failure in hospitalized patients, although the word 'hospitalized' wasn't used, that was implied … and it was indicated for symptomatic relief. I support its use for that indication," said Dr. Wilson Colucci, chief of cardiovascular medicine at Boston Medical Center and Boston University. Further, he agreed with CMS that there is not a sufficient amount of data to support the use of nesiritide as a treatment for chronic heart failure.

However, Dr. Colucci disagreed with Dr. Sackner-Bernstein when it came to removing nesiritide from the market, "at least based on the current data."

"With regard to renal function, there has been a lack of substantial benefit, but relatively very little effect one way or the other when one looks at the totality of the renal effect. That's not the indication, and that's not the reason to give the drug," said Dr. Colucci.

He went on to say that Dr. Sackner-Bernstein's metaanalysis fell short of establishing any kind of risk with the drug.

Dr. Colucci disclosed that he was an investigator involved in the studies that led to nesiritide's FDA approval for treatment of ADHF. ■

Nesiritide Increases Mortality If Acute Renal Failure Occurs

BY ALICIA AULT
Contributing Writer

PHILADELPHIA — Patients with heart failure who are taking nesiritide and who develop acute renal failure may be at an increased risk of death, Dr. Jose Iglesias said at the annual meeting of the American Society of Nephrology.

He presented new data showing that the use of nesiritide in patients with heart failure was not an independent predictor of mortality, but that it may be associated with an increased risk of mortality among patients who develop acute renal failure (ARF) after administration of neseritide.

Nesiritide (Natrecor) fell under scrutiny following the publication in early 2005 of two studies showing that it had no real benefit in heart failure and might increase the risk of death, Dr. Iglesias of the University of Medicine and Dentistry of New Jersey School of Osteopathic Medicine said in presenting two studies on the topic. He conducted the research with associates at his institution, the Community Medical Center of Toms River (N.J.), and the University of Illinois at Chicago.

Both studies looked at patients with heart failure at the Toms River hospital, which admits close to 2,000 patients for that diagnosis each year.

In one study, the researchers analyzed 60-day mortality and ARF risk in 219 consecutive patients who came to the hospital for heart failure, including 71 who were given nesiritide. Overall, there was no significant difference in ARF between patients who received the drug (29%) and those who did not get an infusion (20%). Nor was there a big difference in mortality: 23% for those receiving nesiritide and 16% for those who did not get the drug.

In the nondrug group, lower glomerular filtration rate and older age were independent predictors of ARF. For the nesiritide group, hypertension and elevated blood urea nitrogen/serum creatinine were independent predictors. Mortality predictors in the nesiritide group included brain natriuretic peptide, intensive care admission, blood urea nitrogen/serum creatinine, and digoxin use.

However, 12 patients (23%) died after developing ARF, and 9 of those were taking nesiritide, suggesting an association. The researchers looked for some sort of link and found that among patients who died after developing ARF, the drug was an independent predictor of mortality when they used Cox analysis.

Dr. Iglesias and his colleagues concluded that patients who received nesiritide and who then developed ARF may be at increased risk of death.

In a larger, not-yet-completed investigation, he and his colleagues studied 1,412 heart failure patients, of whom 335 received nesiritide. Of the 1,412 patients, 186 (13%) developed ARF. Among those, 82 (44%) had received nesiritide, which was associated with a significant increase in the risk of ARF (odds ratio of 5.93). Patients who developed ARF also had significantly higher mortality: 18%, compared with 5% for those without ARF (odds ratio of 4).

The independent predictors for ARF were chronic renal failure, inotropic support, and nesiritide. Using a univariate analysis, the researchers found that the independent predictors for mortality included older age, digoxin use, nesiritide, inotropic support, chronic renal failure, and a history of hypertension.

Both Dr. Iglesias and a coauthor, Dr. Lance Berger, receive honoraria from Fremont, Calif.–based Scios Inc., which makes Natrecor. ■

Higher Weight Found Linked to a Decrease in Heart Failure Mortality

DALLAS — Bigger is better for patients with heart failure, Dr. Stefan D. Anker said at the annual scientific sessions of the American Heart Association.

Increased weight was associated with a lower risk of death or hospitalization during nearly 5 years of follow-up in a post hoc analysis of more than 2,500 patients with heart failure.

The finding was consistent with previous reports that showed lower survival rates in heart failure patients who had a relatively low body mass index (BMI), said Dr. Anker, a cardiologist at the National Heart and Lung Institute in London.

"Never tell a patient with a BMI of less than 40 kg/m^2 to lose weight," said Dr. Anker. He used a cutoff of 40 kg/m^2 because little information is available on larger patients.

The analysis used data collected in the Carvedilol or Metoprolol European Trial (COMET), which was designed to compare the efficacy of these two β-blockers in patients with moderate-to-severe heart failure (Lancet 2003;362:7-13). The study enrolled patients with New York Heart Association class II-IV disease and a left ventricular ejection fraction of less than 40%. Of the 3,029 patients in the study, Dr. Anker focused his analysis on 86% of patients who did not have edema at baseline. In addition to being treated with one of the two β-blockers, patients received a full panel of medications for heart failure. They were followed for an average of 58 months.

Mortality among 302 patients whose average BMI was less than 22 during the study was 49%, compared with a rate of 32% in 1,145 patients with BMI averages of 25-29.9 and a rate of 25% in 474 patients with averages of 30 or more during the study.

For every increased unit of BMI, mortality fell by 6%, and the rate of death or hospitalization for heart failure dropped by 2%. Both of these rate reductions were statistically significant, Dr. Anker said.

—Mitchel L. Zoler