

# Drug Usage Evaluation: Nesiritide (Natrecor®)

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## Introduction

Congestive heart failure (CHF) is a condition in which the heart is unable to pump enough blood to meet the needs of the body. Acute decompensated heart failure (ADHF) is an acute worsening of CHF. The patient is acutely ill, generally requires hospitalization, and has significant symptoms such as shortness of air and excess fluid even at rest or with minimal activity. Symptoms are caused by increased blood pressure in the lungs which drives fluid out of the vasculature and into lung fields.[1] Although no consensus guidelines exist for ADHF, treatment is aimed toward improving symptoms, particularly shortness of air.[2]

In 2003, 4.9 million people in the U.S. had CHF. There are 550,000 new cases each year[2] and the incidence of CHF has increased 155% over the past 20 years.[3] These increases are likely due to the growing geriatric population. CHF is a significant source of morbidity and mortality. Over one million U.S. hospital admissions annually are attributed to CHF.[2] Direct and indirect heart failure treatment in the U.S. topped \$24.3 billion in 2003 making it the most expensive hospital admission diagnosis and the single largest expense for Medicare.[1,2,4] Nearly \$500 million is spent annually on heart failure medications.[4]

Nesiritide, a human B-type natriuretic peptide (BNP), is the first new ADHF agent on the market in over 10 years and was approved for use in the U.S. in 2001.[1] The medication binds to a receptor on vascular smooth muscle and endothelial cells and causes dilation of veins and arteries. Nesiritide is indicated for patients with ADHF who have shortness of air at rest or with minimal activity. The medication relieves symptoms by decreasing blood pressure in the lungs and also has a mild diuretic effect. The recommended dose is a 2 mcg/kg intravenous bolus followed by a continuous infusion of 0.01 mcg/kg/min.[5] BNP levels are routinely monitored in patients with ADHF as a marker of severity of illness, however BNP levels should not be ordered for patients receiving nesiritide because nesiritide *is* BNP and the levels will be meaningless. Cost of nesiritide is approximately \$400 per dose.

Based on the high prevalence of CHF, high cost of treatment, administration restrictions and patient monitoring, and limited evidence of effectiveness for other disease states, it is critical that utilization is monitored. This monitoring helps ensure that hospitals and health-care providers are effectively treating their patients in the most cost-effective way. Nesiritide is a fragile peptide, protein that requires careful handling and preparation. Administration of nesiritide must be carefully monitored and used only in the appropriate situations.

The purpose of this drug usage evaluation (DUE) is to evaluate Nesiritide usage at Wesley Medical Center. By review of patient charts and records, two questions will be answered:

1. Does nesiritide administration match the defined protocol at this facility? The defined protocol includes proper patient selection and required monitoring parameters. Outlying uses of the drug will be described, as well as consistencies and inconsistencies in use.
2. What are the outcomes of patients who are treated with Nesiritide? Outcomes will be described as length of hospital stay and mortality.

Based on the findings of the data collection, review of the hospital policy may be indicated.

## Methodology

The study design is a retrospective, non-interventional DUE. The facility under review is Wesley Medical Center, Wichita, Kansas, a 760-bed tertiary care facility and teaching hospital. All patients receiving nesiritide from March 1, 2004 to February 28, 2005 were included in this DUE. Most of the necessary data for this study was collected from the hospital's integrated computer documentation records. Any data missing from the computer documentation was collected from the actual patient charts. This resulted in 115 orders for nesiritide in 106 patients.

## Results:

The average patient age was  $67 \pm 12$  years; 65% of patients were male. The top five co-morbid disease states patients possessed were hypertension, coronary artery disease, smoking, diabetes, and CHF. Nephrology was the primary ordering service (46%), followed by Cardiology (28%), and Cardiovascular Surgery (18%). Nesiritide was initiated during coronary artery bypass graft surgery in 17 patients. The all-cause in-hospital mortality rate was 21%. The hospital's preprinted protocol-based orders were utilized in 77% of patients (89/115). Even with preprinted orders, the administration criteria were completely addressed in only 56% of patients (50/89).

Indications for drug use documented in the patient chart included BNP level  $\geq 400$  (72%), CHF (35%), kidney failure (22%), cardiomyopathy (6%), and fluid overload (3%). No indication was found in the chart in 25% of patients. Prior to nesiritide administration, 21% of patients had contraindications against therapy. The most common side effect, occurring in 51% of patients, was a systolic blood pressure that dropped below 90 mmHg within two hours of administration. Serum creatinine increased by greater than 0.5 mg/dL in 31% of patients, indicating possible acute kidney failure.

The average number of doses per patient was  $3.75 \pm 4.17$ ; average cost per patient was  $\$1587 \pm \$1768$ . A total of 510 infusions were prepared costing \$215,944, however only 416 of these doses were actually administered and charged to the patient. The 94 wasted doses are not reimbursable and resulted in \$39,801 lost product.

**Table 1:** Nesiritide Drug Utilization Evaluation Criteria

Criteria	Expected	Actual
<i>Justification for Use:</i>		
1. Acute Decompensated Heart Failure (ADHF)	100%	35%
<i>Critical Indicators:</i>		
A. Criteria for use met and documented		
1. ADHF (NYHA Class III-IV)	100%	35%
2. BNP level $\geq 400$ pg/mL prior to therapy	100%	72%
B. Dosed appropriately		
100%	48% (bolus); 87% (drip)	
C. Absence of contraindications to therapy		
100%	79%	
D. Length of therapy $\leq 48$ hours		
78%	51%	
E. BNP levels obtained while patient on nesiritide		
0%	30%	
<i>Complications</i>		
1. SBP $< 90$ mmHg on therapy		
11%	51%	
2. Possible kidney failure ( $\uparrow$ in SCr $\geq 0.5$ mg/dL)		
15%	31%	
3. Death		
1.5%	21%	
<i>Outcome Measures</i>		
1. Length of stay		
5.4 days	15.8 days	
2. ICU length of stay		
2.5 days	11.7 days	
3. Readmission for any reason within 30 days		
20%	21%	
4. Readmission for heart failure within 30 days		
7%	6%	

## Discussion:

This was a large, extensive DUE that will provide valuable information to the hospital's Pharmacy & Therapeutics Committee. The committee will now need to discuss mechanisms to increase compliance with use of the preprinted protocol-based orders, appropriate dosing, monitoring, and appropriate indication for use. This may include such mechanisms as physician education, pharmacy intervention for patients falling outside the appropriate use protocol, or restricting the medication to use by certain physicians or physician groups. To reduce hospital costs, the pharmacy department will need to discuss production processes that will reduce the amount of wastage.

## Conclusion

This drug usage evaluation demonstrates that nesiritide is not being used in full accordance with the outlined standards set by the hospital's Pharmacy and Therapeutics Committee. Mechanisms to increase physician compliance and reduce product wastage should be explored.

## References

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