Nesiritide (Natrecor®)
Archived Medical Policy

Archived medical policies are no longer subject to periodic review, are maintained for reference, and may be returned to active status if the need is identified.

Policy # 00085
Original Effective Date: 09/29/2003
Archived Date: 12/15/2010

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider the use of nesiritide (Natrecor®) for the treatment of acutely decompensated congestive heart failure to be eligible for coverage when patient selection criteria are met.

Patient Selection Criteria
Coverage eligibility for the use of nesiritide for treatment of congestive heart failure will be considered when all of the following criteria are met:

- Documented acutely decompensated congestive heart failure; and
- Dyspnea at rest or with minimal activity; and
- Nesiritide is administered intravenously (IV) in the acute care hospital setting; and
- Length of use is limited to 48 hours.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of nesiritide when patient selection criteria are not met to be investigational.*

Based on review of available data, the Company considers the use of nesiritide for non-FDA approved indications to be investigational.*

Background/Overview
Nesiritide is a recombinant form of human B-type natriuretic peptide (rhBNP), a naturally occurring protein secreted by the heart. It has been utilized in the treatment of individuals with acutely decompensated congestive heart failure (CHF) who have dyspnea at rest or with minimal activity. Nesiritide binds to the particulate guanylatecyclase receptor of vascular smooth muscle and endothelial cells, leading to increased intracellular concentrations of cyclic guanosine monophosphate (cGMP) and smooth muscle relaxation.
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cGMP serves as a second messenger to dilate veins and arteries. Studies on individuals with acutely decompensated CHF have shown a reduction in pulmonary capillary wedge pressure (PCWP) and dyspnea when using the recommended dose of nesiritide.

FDA or Other Governmental Regulatory Approval
U.S. Food and Drug Administration (FDA)

Rationale/Source
Nesiritide has been studied in ten clinical trials including 941 patients with CHF (NYHA class II-III 61%, NYHA class IV 36%; mean age 60 years, women 28%). There were five randomized, multi-center, placebo or active-controlled studies (comparative agents included nitroglycerin, dobutamine, milrinone, nitroprusside, or dopamine) in which 772 patients with decompensated CHF received continuous infusions of Natrecor at doses ranging from 0.01 to 0.03µg/kg/min. Of these patients, the majority (n=541, 70%) received the Natrecor infusion for at least 24 hours; 371 (48%) received Natrecor for 24–48 hours and 170 (22%) received Natrecor for greater than 48 hours.

In controlled trials, Natrecor has been used alone or in conjunction with other standard therapies, including diuretics (79%), digoxin (62%), oral ACE inhibitors (55%), anticoagulants (38%), oral nitrates (32%), statins (18%), class III antiarrhythmic agents (16%), beta-blockers (15%), dobutamine (15%), calcium channel blockers (11%), angiotensin II receptor antagonists (6%) and dopamine (4%). Natrecor has been studied in a broad range of patients, including the elderly (>65 years of age), women (30%), minorities (26% black), and patients with a history of significant morbidities such as hypertension (67%), previous myocardial infarction (50%), diabetes (44%), atrial fibrillation/ flutter (34%), nonsustained ventricular tachycardia (25%), ventricular tachycardia/fibrillation (12%), preserved systolic function (9%) and acute coronary syndromes less than seven days before the start of Natrecor (4%).

The VMAC (Vasodilation in the Management of Acute Congestive Heart Failure) trial was a randomized, double blind study of 489 patients (246 patients requiring a right heart catheter, 243 patients without a right heart catheter) who required hospitalization for management of shortness of breath at rest due to acutely decompensated CHF. The study compared the effects of Natrecor, placebo and IV nitroglycerin when added to background therapy (IV and oral diuretics, non-IV cardiac medications, dobutamine and dopamine). Patients with acute coronary syndrome, preserved systolic function, arrhythmia and renal insufficiency were not excluded. The primary endpoints of the study were the change from baseline in PCWP and the change from baseline in patients’ dyspnea, evaluated after three hours. Close attention was also paid to the occurrence and persistence of hypotension, given nesiritide’s relatively long (compared to nitroglycerin) pharmacokinetic (PK) and pharmacodynamic (PD) half-life. In the VMAC study, patients...
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receiving Natrecor reported greater improvement in their dyspnea at three hours than patients receiving placebo (p=0.034).

In a second double-blind study, 127 patients requiring hospitalization for symptomatic CHF were randomized to placebo or to one of two doses of Natrecor (0.015µg/kg/min preceded by an IV bolus of 0.3 µg/kg, and 0.03µg/kg/min preceded by an IV bolus of 0.6µg/kg). The primary endpoint of the trial was the change in PCWP from baseline to six hours, but the effect on symptoms also was examined. In the dose response study, patients receiving both doses of Natrecor reported greater improvement in dyspnea at six hours than patients receiving placebo. The PCWP, right atrial pressure (RAP), CI and other hemodynamic variables were monitored in 246 of the patients in the VMAC trial. There was a reduction in mean PCWP within 15 minutes of starting the Natrecor infusion, with most of the effect seen at three hours being achieved within the first 60 minutes of the infusion.

In several studies, hemodynamic parameters were measured after Natrecor withdrawal. Following discontinuation of Natrecor, PCWP returns to within 10% of baseline within two hours, but no rebound increase to levels above baseline state was observed. There was also no evidence of tachyphylaxis to the hemodynamic effects of Natrecor in the clinical trials.

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.

References

Coding
The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines (BCBSLAMPCG) are obtained from Current Procedural Terminology (CPT®), copyright 2010 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

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Policy History

Original Effective Date: 09/29/2003

09/16/2003  Medical Policy Committee review
09/29/2003  Managed Care Advisory Council approval
10/05/2004  Medical Director review
11/29/2004  Managed Care Advisory Council approval
10/05/2005  Medical Director review
10/18/2005  Medical Policy Committee review. Format revision. No substance change to policy.
10/27/2005  Quality Care Advisory Council approval
07/07/2006  Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
10/04/2006  Medical Director review
12/12/2007  Medical Director review
12/19/2007  Medical Policy Committee approval
12/03/2008  Medical Director review
12/17/2008  Medical Policy Committee approval. No change to coverage eligibility.
12/04/2009  Medical Policy Committee approval
12/16/2009  Medical Policy Implementation Committee approval. The When Services Are Not Covered section was deleted from the policy. Added that if nesiritide is used for non-FDA approved indications, to deny investigational.
12/01/2010  Medical Policy Committee review

Next Scheduled Review Date: Archived Medical Policy.

Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval

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of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
   1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
   2. credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
   3. reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:
   A. in accordance with nationally accepted standards of medical practice;
   B. clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
   C. not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.