B-TYPE NATRIURETIC PEPTIDE (BNP)

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INSTRUCTIONS FOR USE

This Medical Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the enrollee specific document must be referenced. The terms of an enrollee’s document (e.g., Certificate of Coverage (COC) or Summary Plan Description (SPD)) may differ greatly. In the event of a conflict, the enrollee’s specific benefit document supersedes this Medical Policy. All reviewers must first identify enrollee eligibility, any federal or state regulatory requirements and the plan benefit coverage prior to use of this Medical Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

BACKGROUND

B-type natriuretic peptide (BNP) is a peptide produced by cardiac myocytes in response to myocardial stretch and elevated ventricular filling pressures. BNP was originally named brain natriuretic peptide in 1988 because it was first isolated from pig brain. Through cGMP-mediated processes, the hormone indirectly dilates coronary arteries and relaxes myocardium. The peptide has a direct anti-apoptotic effect. BNP’s suppression of aldosterone limits fibrosis after myocardial injury and promotes natriuresis. The precursor prohormone is cleaved to the active form (BNP) and an inert form, an amino-terminal fragment called amino-terminal pro-B-type natriuretic peptide (NT-proBNP). Receptors for BNP exist in the kidney, lung, adipose tissue, adrenal, brain, heart, testis and vascular smooth muscle. The peptide is excreted in the kidney and degraded by endopeptidases in the circulation and by receptors. There are no receptors for NT-proBNP, and it is cleared by renal excretion. Despite the shorter half-life of BNP, the clinical use of BNP and NT-proBNP are comparable, but assay values are different and not interchangeable.
Synthetic BNP is used therapeutically for the management of acute decompensated heart failure. The hormone has protective effects following cardiac ischemic insult and is being investigated in human trials for the preservation of left ventricular structure and function.\(^1\)

Elevated BNP is a marker of increased left ventricular filling pressure and left ventricular dysfunction. Early on, clinical measurement of BNP was applied to the diagnosis of heart failure in the acute setting. The diagnosis of heart failure is problematic. Heart failure (HF) is a syndrome, not a discrete disease, and there are many causes including hypertension, coronary heart disease and diabetes mellitus, to name a few. Key symptoms (dyspnea, fatigue and edema) are common to many clinical conditions, and their differential diagnosis may also include chronic kidney disease, hepatic failure, and pulmonary conditions such as asthma and chronic obstructive pulmonary disease. The definitive diagnosis rests on the combination of clinical observations and tests including laboratory assays, electrocardiography, chest X-ray, and echocardiography, which is an expensive testing modality.

Heart failure accounts for the expenditure of over 35 billion health care dollars annually in the United States.\(^2\) At the Massachusetts General Hospital, length of stay for HF averages 7 days. It has been asserted that a more expeditious diagnosis could decrease the length of hospital stays.\(^3\) Cardiac biomarkers have been studied in an effort to identify a means to hasten diagnosis of HF and reduce costs.

BNP has a positive predictive value of 90% for the diagnosis of HF.\(^4\) The National Academy of Clinical Biochemistry (NACB) states that the use of BNP in the setting of HF decreases cost without increasing risk to patients.\(^5\) The NACB, American College of Cardiology Foundation/American Heart Association Task Force, and Heart Failure Society of America all support the use of BNP for the diagnosis of HF in their practice guidelines.\(^5-7\) A commonly used cut-off for the general patient population is that a BNP of <100 pg/ML or a blood NT-proBNP of <300 pg/mL suggests HF can be ruled out.\(^5\)

The National Academy of Clinical Biochemistry Laboratory Medicine guidelines recommend:\(^5\):

- Using BNP for ruling out or confirming a diagnosis of HF when signs and symptoms are ambiguous in the acute setting.
- Using BNP to rule out the diagnosis of HF in patients with symptoms suggestive of HF in the non-acute setting.

Guidelines from the American College of Cardiology Foundation/American Heart Association Task Force (ACCF/AHA) make the following recommendations for the use of BNP in the diagnosis of HF\(^6\):

- In the urgent care setting, BNP is useful to make a diagnosis of HF.
- In patients with dyspnea, BNP is a useful assay but should not be used alone to make a diagnosis of HF.

The guidelines from the Heart Failure Society of America (HFSA) use language that is more dogmatic\(^7\):

- It is recommended BNP or NT-proBNP levels be assessed in all patients suspected of having HF, especially when the diagnosis is not certain. This recommendation was made on the basis of
randomized, controlled, clinical trials.

- In patients with worsening HF, BNP or NT-proBNP is recommended in patients with dyspnea who are being evaluated for a diagnosis of acute decompensated heart failure. The interpretation of this assay should take into consideration cardiac and noncardiac factors that can alter BNP levels.

The background discussion of the second recommendation includes the Breathing Not Properly study for BNP and the PRIDE study for NT-proBNP.

The NACB also established a committee to review the use of cardiac biomarkers in patients where the biomarker elevation is not limited to acute coronary syndrome or HF. These guidelines take into account patients with kidney disease. It has been estimated that 30% of patients with cardiovascular disease have chronic kidney disease and cardiac biomarkers are often elevated in this patient population. BNP has been found useful for risk stratification in patients with diabetes mellitus type II, chronic kidney disease and anemia; elevation is correlated with development of end stage renal disease.

The NACB guidelines for measuring BNP in patients with chronic kidney disease state:

- In renal failure patients, BNP can be used in the acute setting to aid in the diagnosis of HF for patients with confounding signs and symptoms but cutoff values should be changed for patients with decreased glomerular filtration rates.

The NACB guideline authors note that reference intervals for BNP for patients with chronic renal failure have not been agreed upon and large studies are necessary to establish cutoffs.

BNP and NT-proBNP are both useful for the diagnosis of HF, but BNP should not be measured to diagnose HF in patients who are being treated with synthetic BNP. In terms of diagnostic utility, the marker has also been used to distinguish between constrictive pericarditis and restrictive cardiomyopathy. While BNP is broadly recommended for the diagnosis of HF, there are some situations where BNP may not detect HF, such as right heart failure, NYHA class 2, obesity, and diastolic failure. Other diagnostic limitations include biologic variability and the need for careful interpretation of BNP levels in patients with pulmonary disease, discussed below. BNP is not recommended for screening of HF in asymptomatic patients.

Levels of BNP correlate with New York Heart Association class, and there is evidence that BNP is useful for risk stratification in patients with HF. The NACB practice guidelines state that BNP and NT-proBNP can provide useful information in selected situations where risk stratification is necessary. The ACCF/AHA guidelines also state that BNP and NT-proBNP can be useful in risk stratification.

Given that effective therapy of HF decreases BNP concentration, some clinicians already use serial monitoring of BNP to titrate therapy in HF patients, and the use of cardiac biomarkers to drive treatment decisions for HF has been compared to the use of prostate specific antigen to drive treatment decisions for prostate cancer patients. Studies assessing the benefit of serial BNP measurements for treatment titration have been ongoing for over a decade. Results of the first studies were equivocal. In the 2009 guidelines, the ACCF/AHA Task Force stated conclusive evidence was lacking to prove that serial BNP measurements could be used to titrate therapy. They graded the value of the use of serial measurements of BNP to guide therapy, level of evidence C, meaning that certainty derived only from consensus opinion of experts or standard of care. The guideline...
authors stated that ongoing trials would resolve the role of BNP in HF management. Since the time of those guidelines, the PROTECT trial reported that biomarker-guided therapy is superior to standard of care therapy.\textsuperscript{16} PROTECT (Use of NT-proBNP Testing to Guide Heart Failure Therapy in the Outpatient Setting) was a randomized, controlled trial which compared the occurrence of adverse outcomes such as cardiac death and hospitalization for HF in the control group that received standard of care therapy per consensus guidelines with adverse outcomes in the BNP arm, which received standard therapy guided by a goal to sustain NT-proBNP concentrations to less than or equal to 1000 pg/ML.\textsuperscript{16} The study found a decrease in adverse outcomes in the patients who had biomarker-guided therapy.

The use of BNP for diagnosis, risk stratification, and management of pulmonary disease has been less well established but has been studied nonetheless. The marker has been useful as a “rule out” test in the diagnosis of pulmonary embolism and in the prediction of adverse outcomes in patients with pulmonary embolism. BNP may have a future role in the titration of therapy in patients with pulmonary hypertension. Pleural fluid BNP may be useful clinically to distinguish exudates from transudates. BNP may be useful for risk stratification in community-acquired pneumonia.\textsuperscript{17}

Marked elevations of BNP occur in Kawasaki disease, a syndrome that mainly affects the pediatric population with complications that can lead to cardiac death. The diagnosis of Kawasaki disease is complex and is based on the presence of fever and the identification of a constellation of clinical findings. In a recent study, patients with incomplete diagnostic criteria for Kawasaki disease had higher NT-proBNP levels than febrile controls.\textsuperscript{18} Larger studies may show that NT-proBNP has utility for the diagnosis of Kawasaki disease.

POLICY

For the following CPT code(s) in Table 1, the patient should have a diagnosis (ICD-10-CM) code(s) listed in the attached files below.

\textit{Table 1. HCPCS Codes (Alphanumeric, CPT\textsuperscript{\textregistered} AMA)}

<table>
<thead>
<tr>
<th>HCPCS Code</th>
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<tr>
<td>83880</td>
<td>B type natriuretic peptide</td>
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\textit{ICD-10 Diagnosis Codes (Proven)}

CMP-025 BNP ICD10 v1.1
REFERENCES


<table>
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<tr>
<td>12/07/2017</td>
<td>Annual Policy Review Completed – Updated ICD10 codes as per CMS recommendations.</td>
</tr>
<tr>
<td>01/21/2017</td>
<td>Updated ICD10 codes as per CMS recommendations. Removed ICD9 code file.</td>
</tr>
<tr>
<td>10/01/2015</td>
<td>Removed ICD9 table. Embedded ICD9/ICD10 PDF files.</td>
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