



Australian Government

Department of Health and Ageing



Australia and New Zealand Horizon Scanning Network

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AN INITIATIVE OF THE NATIONAL, STATE AND
TERRITORY GOVERNMENTS OF AUSTRALIA
AND THE GOVERNMENT OF NEW ZEALAND

National Horizon Scanning Unit

Horizon scanning prioritising summary

Volume 4, Number 6:

**Elecsys[®] proBNP Immunoassay: For the
diagnosis of congestive heart failure.**

February 2004



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The production of this *Horizon scanning prioritising summary* was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from health departments in all states and territories, the Australia and New Zealand governments; MSAC and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

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PRIORITISING SUMMARY

REGISTER ID: 000087

NAME OF TECHNOLOGY: ELECSYS[®] PROBNP IMMUNOASSAY

PURPOSE AND TARGET GROUP: FOR THE DIAGNOSIS OF CONGESTIVE HEART FAILURE

STAGE OF DEVELOPMENT (IN AUSTRALIA):

- | | |
|---|---|
| <input checked="" type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established |
| <input type="checkbox"/> Experimental | <input type="checkbox"/> Established <i>but</i> changed indication or modification of technique |
| <input type="checkbox"/> Investigational | <input type="checkbox"/> Should be taken out of use |
| <input type="checkbox"/> Nearly established | |

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- | | |
|--|---|
| <input type="checkbox"/> Yes | ARTG number |
| <input checked="" type="checkbox"/> No | <input type="checkbox"/> Not applicable |

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Austria	✓		
United States	✓		
Germany	✓		
Japan	✓		

IMPACT SUMMARY:

Roche Diagnostics manufacture the Elecsys[®] proBNP Immunoassay and Biosites[®] Diagnostics Incorporated manufacture the Biosite[®] Triage BNP. Both are tests for the diagnosis of congestive heart failure, however only the Elecsys[®] proBNP Immunoassay is fully automated. Both products received a 510(k) pre-market notification from the United States FDA in December 2003, however neither product has TGA approval in Australia. If given approval, it is likely that these tests would be provided through public and private pathology laboratories for the diagnosis of patients suspected of heart failure.

Limited information is available on the Biosite[®] Triage BNP assay, therefore this summary will concentrate on the Roche Diagnostics Elecsys[®] proBNP Immunoassay.

Heart failure occurs when the heart is unable to pump blood adequately to the rest of the body, which may lead to the accumulation of fluid in the lungs or legs. Causes of heart failure include chronic hypertension, cardiomyopathy and myocardial infarction. In Australia, heart failure occurs predominantly amongst those aged 75 and over and accounted for 40,942 hospitalisations and 2,612 deaths, during the period 2000-01 (AIHW 2003). The number of public hospital separations in Australia for patients with heart failure and shock, with and without catastrophic

complications and comorbidities, were 8,632 and 30,873, respectively, in 2001-02, (AR-DRG numbers F62A and F62B, respectively) (AIHW 2004).

Recent developments have led to the measurement of circulating levels of brain natriuretic peptide (BNP) as a frontline diagnostic aid to identify patients with elevated ventricular filling pressure. BNP is an active peptide with vasodilating and natriuretic (elimination of extra sodium in urine) properties. Despite its name, the majority of circulating BNP is secreted by cardiomyocytes in response to wall stretch or ventricular tension. The amino, or N-terminal end (NT) of the precursor to BNP, pro-BNP, is secreted in equal proportions to BNP, has a longer half-life, and therefore increased sensitivity. It has been proposed as an accurate marker for the assessment of heart failure (Yeo et al 2003, Pfister et al 2004, Seino et al 2004). Early detection of heart failure, especially in an emergency situation, may enable early treatment and improve patient outcomes. The Elecsys[®] proBNP Immunoassay is an electrochemiluminescent immunoassay which uses purified synthetic NTG-proBNP as a reference standard and can be used on human serum and plasma. The assay takes approximately 20 minutes to complete.

This assay is not designed as a screening tool but for testing of individuals suspected of having congestive heart failure. Cardiac and pulmonary patients present with similar symptoms such as shortness of breath and most will undergo an exploratory electrocardiogram to ascertain the cause of symptoms (Maisel et al 2003). It is hoped that through the use of this assay, patients suffering from pulmonary rather than cardiac symptoms will be excluded so that the number of exploratory cardiograms will be reduced.

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Pfister et al (2004) analysed samples from 339 consecutive patients undergoing investigative cardiac catheterisation (level 1b, diagnostic levels of evidence, see Appendix A). Depending on the severity of left ventricular dysfunction, the diagnostic accuracy (area under the curve) for NT-proBNP ranged from 0.71 to 0.83, the sensitivity from 88% to 92%, specificity from 37% to 61%, positive predictive value from 15% to 72% and negative predictive value from 74% to 99%.

Similar results were reported in the study by Seino et al (2004) where plasma concentrations of NT-proBNP from 67 healthy controls were compared to the plasma concentrations of 105 consecutive patients with chronic heart failure (level 3b, diagnostic level of evidence) (Table 1). Both NT-proBNP and BNP levels rose with indicators of severity of heart disease, such as the New York Heart Association (NYHA) classification of heart failure (I mild, IV severe) and reduced left ventricular ejection fraction (LVEF%) (Figure 1). There was significant correlation between levels of NT-proBNP and BNP ($r=0.737$, $p<0.001$). The diagnostic accuracy for LVEF <40% and <50% (area under the curve) was 0.754 and 0.820 for NT-proBNP, respectively. The specificity and sensitivity for the Roche Elecsys[®] proBNP Immunoassay were 73% and 85%, respectively.

Table 1 Results from Seino et al (2004)

Controls	NYHA I	NYHA II	NYHA III	NYHA IV
N=67	N=19 LVEF% = 57.5 BNP pg/ml = 24.9	N=50 LVEF% = 53.2 BNP pg/ml = 105.9	N=25 LVEF% = 44.3 BNP pg/ml = 388.3	N=9 LVEF% = 33.0 BNP pg/ml = 1,438
NT-proBNP pg/ml = 55	NT-proBNP pg/ml = 25	NT-proBNP pg/ml = 622	NT-proBNP pg/ml = 2,241	NT-proBNP pg/ml = 10,018

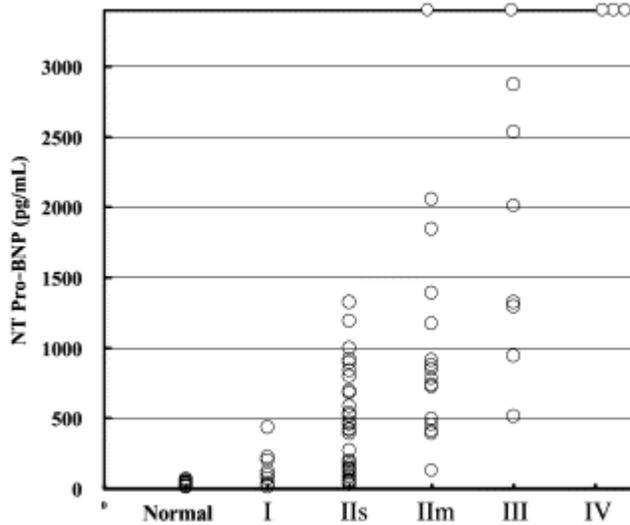


Figure 1 Levels of NT-proBNP versus New York Heart Association classification of heart failure (I mild, IV severe) (Seino et al 2004).

The Elecsys[®] proBNP Immunoassay may be analysed utilising the Roche Diagnostics Elecsys 1010 or 2010 analysers. The Elecsys 1010 and 2010 are capable of routinely conducting a number of different diagnostic assays for the detection of thyroid, cardiac, anaemia, hepatitis, fertility, and tumour markers, and are currently in widespread use in diagnostic laboratories in Australia. The Elecsys 1010 and 2010 are capable of determining 58 and 86 samples per hour (Figure 2).



Figure 2 The Elecsys 1010 analyser (Printed with permission, Roche Diagnostics)

The Elecsys 1010 costs approximately A\$50,000. The price of the Elecsys NT-proBNP kit is currently unavailable for Australia.

The current tool for the diagnosis of heart failure and the assessment of cardiac function is the echocardiogram, which utilises ultrasound to image the heart and surrounding tissues, providing structural and functional information. The number of claims processed by the HIC for the

Medical Benefit Schedule number 55113 (echocardiograph for the investigation of symptoms or signs of cardiac failure) was 237,106 for the period July 2002- June 2003. The Medicare Benefits Schedule fee for this procedure is \$230.

CONCLUSION:

There is limited level 1b evidence (diagnostic levels of evidence) on the Elecsys® proBNP Immunoassay, however the potential uptake of the technology is high. It appears that this test may be a useful adjunct in the rapid diagnosis of heart failure, although with apparently low test specificity.

HEALTHPACT ACTION:

It is therefore recommended that a Horizon Scanning report be conducted.

SOURCES OF FURTHER INFORMATION:

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- Phillips, B., Ball, C. et al (2001). *Oxford Centre for Evidence-Based Medicine Levels of Evidence (May 2001)* [Internet]. Centre for Evidence-Based Medicine, Oxford, UK. Available from: http://www.cebm.net/levels_of_evidence.asp [Accessed 28th January 2004].

SEARCH CRITERIA TO BE USED:

- Atrial Natriuretic Factor/*blood
- Biological Markers/blood
- Natriuretic Peptide, Brain/*blood
- Nerve Tissue Proteins/*blood
- Peptide Fragments/*blood
- Protein Precursors/*blood
- Ventricular Dysfunction, Left/*blood/*diagnosis