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Australia and New Zealand Horizon Scanning Network

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# **National Horizon Scanning Unit**

## **Horizon scanning prioritising summary**

**Volume 6, Number 12:**

**FibroTest-ActiTest: A diagnostic test for  
liver fibrosis in patients with hepatitis C.**

**August 2004**



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# PRIORITISING SUMMARY

**REGISTER ID:** 000120

**NAME OF TECHNOLOGY:** FIBROTEST-ACTITEST

**PURPOSE AND TARGET GROUP:** A DIAGNOSTIC TEST FOR LIVER FIBROSIS IN PATIENTS WITH HEPATITIS C

## 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
France	✓		
Australia	✓		

## IMPACT SUMMARY:

Biopredictive have developed a non-invasive alternative to liver biopsy, the FibroTest-ActiTest. FibroTest-ActiTest is a diagnostic blood test for liver fibrosis for patients infected with hepatitis C. The test is currently unavailable in Australia but is in limited use in some European countries.

## BACKGROUND

Hepatitis C is a blood-borne disease of the liver caused by the hepatitis C virus (HCV). The presence of anti-HCV antibody in serum of a patient indicates infection with the hepatitis C virus. Patients may be unaware that they are infected for some time, as acute symptoms are rare. In Australia, people infected with HCV must demonstrate a minimum stage of fibrosis on liver biopsy to qualify for the standard combination antiviral therapy. Therefore it is recommended that patients undergo a liver biopsy for the adequate management of hepatitis C (Rossi et al 2003).

FibroTest-ActiTest is a minimally invasive blood test that may be used as an alternative to liver biopsy. The FibroTest-ActiTest uses a combination of six serum biochemical markers ( $\alpha_2$ -macroglobulin, haptoglobin,  $\gamma$ -glutamyltranspeptidase, total bilirubin, apolipoprotein A1 and alanine aminotransferase) to assess the extent of liver fibrosis (FibroTest) and necroinflammatory activity (ActiTest). The test utilises an algorithm to combine the biochemical marker results obtained from standard diagnostic laboratory tests, with the

patient's age and gender to give a numeric quantitative estimate of liver fibrosis ranging from 0 to 1, with scores >0.6 considered to represent significant fibrosis (Poynard et al (2004).

#### **CLINICAL NEED AND BURDEN OF DISEASE**

It is estimated that there over 200,000 people in Australia are infected with the hepatitis C virus, with about 11,000 new infections occurring each year (Australian Government Department of Health and Ageing 2004). It is likely that prevalence of hepatitis C is underestimated due to the numbers of people with hepatitis C who are currently asymptomatic (Australian Government Department of Health and Ageing 2004).

Of annual total notifications to the National Notifiable Diseases Surveillance System between 1991 and 2000, approximately 65% of people diagnosed with HCV were aged between 20-39 years, with approximately 35% of all diagnoses in women. Approximately 75% of individuals infected with HCV will remain infectious and at risk of developing long-term sequelae, such as cirrhosis of the liver (7% of infected individuals). Rates of liver failure and hepatocellular carcinoma following cirrhosis have been estimated to be four and one percent, respectively (Australian National Council on AIDS, Hepatitis C and Related Diseases Hepatitis C Sub-Committee 2002).

Projections of the number of people living with HCV-related cirrhosis, incident cases of liver failure and hepatocellular carcinoma, and cumulative numbers of HCV related deaths were all projected to at least treble by 2020 (Australian National Council on AIDS, Hepatitis C and Related Diseases Hepatitis C Sub-Committee 2002).

The number of public hospital separations in Australia for chronic and acute viral hepatitis C (AR-DRG numbers B18.2 and B17.1) was 2,047 and 177, respectively, during the year 2001-02 (AIHW 2004).

#### **DIFFUSION**

FibroTest-ActiTest is currently unavailable in Australia although a preliminary study has been conducted here. FibroTest-ActiTest is available in some European countries and it is expected to be released in the United Kingdom in 2004. FibroTest-ActiTest will be released in the United States in 2004 as HCV FibroSure (National Horizon Scanning Centre 2004).

#### **COMPARATORS**

The gold standard for the assessment of HCV-related fibrosis and necro-inflammatory activity in the liver is liver biopsy. Liver biopsy is highly invasive and approximately 0.3% of patients develop substantial complications. In addition, liver biopsy is prone to sampling error due to the possibility of heterogenous distribution of pathology in the liver (Rossi et al 2003).

#### **EFFECTIVENESS AND SAFETY ISSUES**

A study (level 1 diagnostic levels of evidence) has been conducted in Australia, validating the accuracy of the FibroTest-ActiTest. Serum was obtained from 125 consecutive patients with confirmed hepatitis C who had undergone liver biopsy. The prevalence of fibrosis in this patient group was 0.38, determined by liver biopsy. The negative predictive value of a FibroTest score of <0.1 was reported as 85% and the positive predictive value of a FibroTest score >0.6 (significant fibrosis) was 78%. Thirty-three of the 125 patients had FibroTest scores of <0.1, however six of these patients (18%) were false negatives who had significant fibrosis as determined by liver biopsy. Conversely, 24/125 (19%) patients had FibroTest scores of >0.6 (significant fibrosis), of these 5 (21%) had mild fibrosis determined by liver biopsy. Of the 125 patients enrolled in the study, 57 (46%) could have avoided liver biopsy, however discrepant results were recorded for 11 of those 57 (19%) (Rossi et al 2003).

The cross-classification study by Poynard et al (2004) reported on the discrepancies between the FibroTest-ActiTest and the reference standard liver biopsy, in 537 patients with confirmed hepatitis C (level 2 diagnostic levels of evidence). Discordance between the two results was reported for 154/537 (29%) patients, and was attributed to failure of biopsy (poor quality) or the FibroTest-ActiTest, or both. For patients whose results were discordant due to failure of the FibroTest-ActiTest, there were seven (1.3%) false negatives and six (1.1%) false positives. However, 97 patients experienced biopsy failure with 77 (14%) false negatives and 22 (4.1%) false positives.

Several other studies have been published that have assessed the comparison of the FibroTest-ActiTest to liver biopsy, however the authors of this summary were unable to access these articles. These studies were assessed by the National Horizon Scanning Centre (2004) who found that their results supported the use of the FibroTest-ActiTest as an alternative to liver biopsy. However, due to changing clinical practice in the United Kingdom (reduction of the number of liver biopsies performed in favour of routine antiviral therapy), it was felt that the need for the FibroTest-ActiTest would be reduced.

### **COST IMPACT**

The cost of the FibroTest-ActiTest is approximately £70 (\$180 on the 12<sup>th</sup> August 2004) per test National Horizon Scanning Centre (2004). The current Medicare Benefits Schedule fee for percutaneous liver biopsy is \$145 (item number 30409). In addition, there may be associated costs involved in the performance of a liver biopsy such as the cost of an inpatient stay in hospital.

### **ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS**

No issues were identified/raised in the sources examined.

### **OTHER ISSUES**

The first author of '*Prospective Analysis of Discordant Results between Biochemical Markers and Biopsy in Patients with Chronic Hepatitis C*', Poynard, is a consultant and has a capital interest in Biopredictive.

### **CONCLUSION:**

There is conflicting high level of evidence (level 1 and 2 diagnostic levels of evidence) describing the effectiveness of the FibroTest-ActiTest. However, there is a rapidly increasing population of individuals with hepatitis C in Australia, and therefore it is anticipated there would be a high uptake of the FibroTest-ActiTest.

### **HEALTHPACT ACTION:**

Therefore it is recommended that this technology be monitored.

### **SOURCES OF FURTHER INFORMATION:**

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Australian Government Department of Health and Ageing 2004 *Commonwealth action on hepatitis C - How many people are affected by hepatitis C?* [Internet] Available from: [http://www.health.gov.au/pubhlth/strateg/hiv\\_hepc/hepc/affected.htm](http://www.health.gov.au/pubhlth/strateg/hiv_hepc/hepc/affected.htm) [Accessed 5th August 2004].

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Halfon, P., Imbert-Bismut, F. et al (2002). 'A prospective assessment of the inter-laboratory variability of biochemical markers of fibrosis (FibroTest) and activity (ActiTest) in patients with chronic liver disease', *Comp Hepatol*, 1 (1), 3.

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National Horizon Scanning Centre (2004). *FibroTest-ActiTest, a diagnostic test for liver fibrosis in patients with hepatitis C* [Internet]. Available from: <http://www.publichealth.bham.ac.uk/horizon/2004reports/FibroTests.pdf> [Accessed 11<sup>th</sup> August 2004].

Poynard, T., Munteanu, M. et al (2004). 'Prospective Analysis of Discordant Results between Biochemical Markers and Biopsy in Patients with Chronic Hepatitis C', *Clin Chem*, 50 (8), 1344-1355.

Rossi, E., Adams, L. et al (2003). 'Validation of the FibroTest biochemical markers score in assessing liver fibrosis in hepatitis C patients', *Clin Chem*, 49 (3), 450-454.

**SEARCH CRITERIA TO BE USED:**

Aspartate Aminotransferases/blood  
Hepatitis C, Chronic/\*complications  
Human  
Liver Cirrhosis/blood/\*diagnosis/pathology/\*virology