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Horizon Scanning Technology Prioritising Summary

Wearable artificial kidney (WAK): Portable dialysis for patients with chronic kidney disease

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PRIORITISING SUMMARY

REGISTER ID: **000428**

NAME OF TECHNOLOGY: **WEARABLE ARTIFICIAL KIDNEY (WAK)**

PURPOSE AND TARGET GROUP: **PORTABLE DIALYSIS FOR PATIENTS WITH CHRONIC KIDNEY DISEASE**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☒	Yet to emerge	☐	Established
☐	Experimental	☐	Established *but* changed indication or modification of technique
☐	Investigational	☐	Should be taken out of use
☐	Nearly established		

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☐	Yes	ARTG number
☒	No	
☐	Not applicable	

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Italy	✓		
United States	✓		
United Kingdom	✓		

IMPACT SUMMARY:

Xcorporeal Inc (United States) provides the wearable artificial kidney (WAK) with the aim of providing portable continuous and unobtrusive dialysis. The technology would be available through nephrologists for patients with chronic kidney disease.

BACKGROUND

Chronic kidney disease (CKD) is marked by long-term and usually irreversible loss of kidney function. Initial evidence of kidney damage or reduction in kidney function can be detected by routine blood or urine testing with the most common indicators of kidney damage being elevated protein levels in the urine (proteinuria or albuminuria), blood in the urine (haematuria) or raised blood levels of the waste products of protein metabolism such as urea or creatinine. Kidney function is measured by the glomerular

filtration rate (GFR), a measure of the amount of blood the kidneys clear of waste products in one minute (AIHW 2005).

Chronic kidney disease is classified into five stages of disease severity based on evidence of kidney damage and the degree of kidney function reduction, classified by GFR:

- Stage 1: Kidney damage with GFR at least 90 mL/min/1.73 m2. People with stage 1 CKD have evidence of kidney damage (structural or functional abnormalities of the kidney), but without decreased GFR. There are usually no symptoms.
- Stage 2: Kidney damage with GFR 60 to 89 mL/min/1.73 m2. People with stage 2 CKD have evidence of kidney damage with some reduction in GFR. Most patients at this stage have no symptoms but may have high blood pressure and laboratory abnormalities indicating dysfunction in other organs.
- Stage 3: GFR 30 to 59 mL/min/1.73 m2. People with stage 3 CKD have a significant reduction in GFR. They may or may not show other signs of kidney damage. Blood tests will show increased levels of urea and creatinine, and there may be evidence of dysfunction in other organs. Patients may have symptoms, however they often remain asymptomatic even though their kidney function may be reduced by as much as 70 per cent.
- Stage 4: GFR 15 to 29 mL/min/1.73 m2. People with stage 4 CKD have severely reduced kidney function. Blood levels of urea and creatinine are increased, and there is greater evidence of dysfunction in other organs. Patients usually have only mild symptoms.
- Stage 5: GFR less than 15 mL/min/1.73 m2. In most cases, stage 5 CKD is marked by a range of symptoms and laboratory abnormalities in several organ systems, collectively referred to as uraemia. Patients at this stage may need to be prepared for kidney replacement therapy (dialysis or transplant), which will be required when kidney function is no longer sufficient to sustain life (AIHW 2005).

Patients with chronic kidney disease (stage 5) or end-stage renal disease (ESRD) usually receive dialysis three times per week in a specialist renal unit. More frequent haemodialysis has been demonstrated to be beneficial to ESRD patients in terms of both survival and quality of life. Benefits for patients include less hypertension, reduced cardiovascular disease, improved patient appetite and nutrition, improved serum albumin levels, improved anaemia and a decrease in the incidence of stroke. All of these factors result in a reduced morbidity and mortality in ESRD patients. Therefore, it has been proposed that a wearable dialysis unit would be of great benefit to ESRD patients (Davenport et al 2007; Gura et al 2005).

Although the wearable artificial kidney (WAK) is designed to be used for continuous renal replacement therapy 24-hours per day, seven days per week, it would most likely to be used between 4-8 hours per day. The filtration device is worn on a belt around the waist and weighs approximately five kilograms (Figure 1). There are four micro-pumps which are driven by standard batteries. One pump regulates the ultra-filtration unit whilst the remaining pumps infuse heparin into the blood circuit and infuse sodium bicarbonate, magnesium and calcium acetate into the dialysate circuit. The device is attached to the patient using the standard vascular access used by normal dialysis (fistula needles or central venous access catheters). Safety measures stop the ultra-filtration pump if blood flow ceases due to disconnection of the arterial needle and the blood pump is stopped if air enters the blood circuit system (Davenport et al 2007; Ronco et al 2008).

Figure 1 The wearable artificial kidney (Arcaro 2009; Davenport et al 2007)

The circuit consists of two basic sections (Figure 2). The blood compartment takes blood from the patient to the dialyser and then returns the blood to the patient. The dialysate compartment is where fresh dialysate enters the dialyser and then exits to a series of sorbent canisters where it is regenerated and bicarbonate is added (Davenport et al 2007). The three sorbent canisters contain urease, activated charcoal, and both hydroxyl zirconium oxide and zirconium phosphate. The dialysate is regularly tested for sterility and for ammonia to ensure that they have not become saturated (Ronco et al 2008).

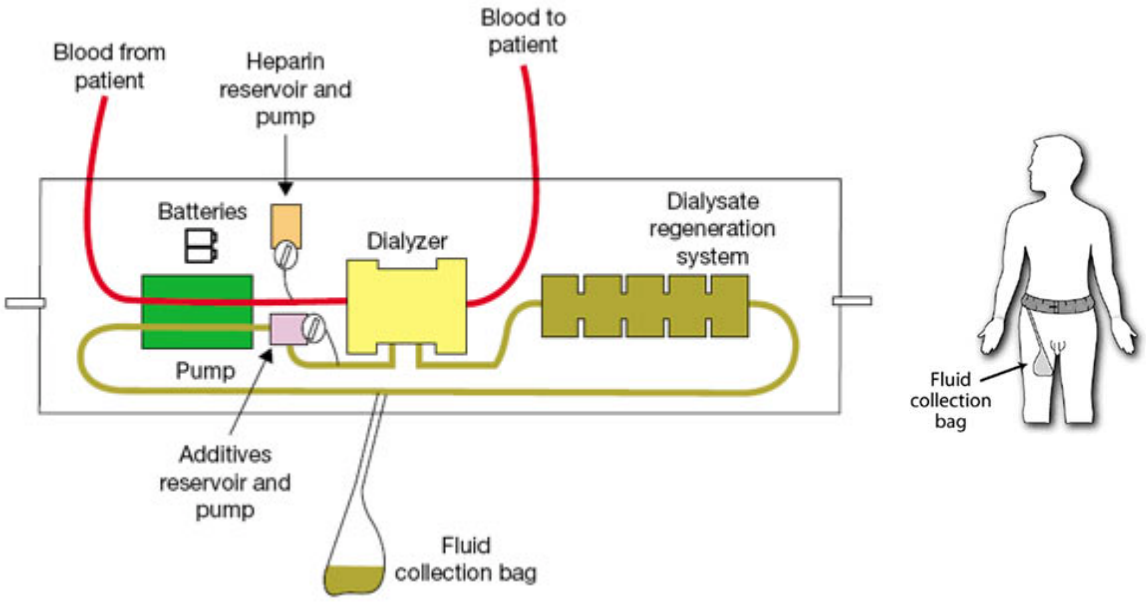

Figure 2 The basic principles of the WAK device (medGadget 2007)

CLINICAL NEED AND BURDEN OF DISEASE

In Australia one in three people are at risk of developing CKD, with one in seven having CKD and one in 1,400 requiring dialysis or a kidney transplant. CKD is the seventh highest cause of death in Australia. The need for dialysis is increasing within the Australian population due to the increasing incidence of diabetes and the ageing population. Over the past 25 years Australian population growth has been less than 40 per cent yet the need for dialysis and kidney transplants has increased 400 per cent. In 2006 there were 9,182 dialysis patients in Australia (Kerr et al 2008). In 2005 around 13 per cent (800) of haemodialysis patients dialysed at home (KHA 2005). It is estimated that the current cost of providing dialysis for one patient for a year costs AUD$60,000. Including transplants the cost of end stage kidney disease is estimated to be at least AUD$570 million annually (KHA 2006a; KHA 2006b). In Australia during 2003-04, eleven per cent of all hospital separations were for dialysis. CKD was recorded as the underlying cause of death in 2,431 cases during 2003. In addition, CKD was recorded as an associated cause of death in an additional 9,217 cases, mostly with cardiovascular disease recorded as a comorbidity (AIHW 2005).

Incidence and prevalence rates of CKD were slightly higher in New Zealand when compared with Australian rates. In 2002, the incidence of renal replacement therapy (RRT) in New Zealand was approximately 120 per million people, compared to 95 in Australia. The prevalence was approximately 680 per million people (pmp) compared to the Australian prevalence of 640. As stated previously, the incidence rate and prevalence of CKD has been increasing steadily over time. In New Zealand the incidence of RRT has increased from approximately 75 pmp in 1995 to 120 pmp in

2002, and prevalence has increased from 350 pmp to 680 pmp over the same time period (KHA 2006a).

DIFFUSION

The wearable artificial kidney is not available in Australia or New Zealand.

COMPARATORS

Australia and New Zealand already have one of the highest rates of home dialysis in the world, however the majority of dialysis is still centre (hospital or clinic) based, with patients usually receiving dialysis three times per week (Agar 2008). It is increasingly recognised that centre based haemodialysis is not the optimum patient management strategy regarding both health outcomes and patient survival times (ANZDATA 2006). As previously stated, more frequent haemodialysis is beneficial to ESRD patients both in terms of survival and quality of life and has been shown to be associated with decreases in mortality and RRT associated morbidity such as cardiovascular disease (Masterson 2008).

SAFETY AND EFFECTIVENESS ISSUES

Initial testing of a smaller WAK device (2.27 kg) was conducted on 12 pigs with ligated ureters, divided into two groups based on weight: group 1 (74.9 ± 1.2 kg) with a blood flow of 44 ml/min and group 2 (47.9 ± 1.7 kg) with a blood flow of 75 ml/min. The animals were dialysed for eight hours with an average dialysate flow of 73 and 85 ml/min in group one and two, respectively. No adverse events were recorded on any of the animals and effective removal of solutes and excess fluid from the uremic animals was achieved (Table 1). Similar clearance rates were reported in both groups despite differences in initial weight.

Table 1 Dialysis results (mean ± SD)

	Group I	Group II
Effective urea clearance, ml/min	24.3 ± 1.4	23.9 ± 3.5
Effective creatinine clearance, ml/min	25.5 ± 1.4	24.7 ± 3.2
Total urea removal, g	12.7 ± 2.8	12.0 ± 2.9
Total creatinine removal, g	0.9 ± 0.2	1.0 ± 0.1
Total phosphorous removal, g	0.8 ± 0.2	0.84 ± 0.4
Total potassium removal, mmol	71.9 ± 13.3	89.1 ± 25.7
Extrapolated standard Kt/V urea	5.4 ± 2.4	8.4 ± 1.5

Kt/V quantifies haemodialysis treatment adequacy. K = urea clearance, t = dialysis time, V = patient's total body water

The only published study using the WAK device is a small, proof-of-concept case series of eight patients with ESRD (level IV intervention evidence). All patients were

currently being treated with conventional haemodialysis three times per week and had been receiving RTT for an average of 17.9 years (range 4-29 years). The average age of the group was 51.7 ± 13.8 years (range 26-67 years). The cause of CKD was glomerulonephritis (n=4), polycystic kidney disease (n=3) and obstructive uropathy (n=1). Due to the experimental nature of the study, the ethics committee required that all patients still underwent conventional intermittent haemodialysis. Patients were weighed before and after treatment and their blood oxygen and cardiac measures were monitored continuously. Ethics required that initially only a maximum of four patients could be treated for four hours. After the successful implementation of this phase, treatment could be extended up to a maximum of eight hours (Davenport et al 2007).

All patients reported on the device favourably with no complaints and would recommend it as a treatment option. Five patients attempted to sleep whilst wearing the device and reported no difficulties. Dialysis outcomes are summarised in Table 2. Concentrations of serum electrolytes and cardiac parameters remained stable and unchanged throughout dialysis. Several times bubbles of carbon dioxide[1] accumulated in the dialysate circuit, creating difficulty with the dialysate flow, but this did not result in the cessation of treatment. One patient experienced clotting of the central venous access catheter when partial thromboplastin time fell to 45 seconds (normal 26-36 seconds) and treatment was discontinued after seven hours. Clotting also occurred in another patient, however this patient was scheduled to terminate treatment at four hours and the partial thromboplastin time had been allowed to fall to ensure that bleeding did not occur upon removal of dialysis needles. Another patient experienced a temporary disconnection when a fistula needle dislodged. This was detected by the WAK's safety mechanism with the needle reinserted and treatment continued.

Further dialysis outcomes were reported in a later paper by Gura et al (2009) and are summarised in the lower section of Table 2. In patients on long-term dialysis, β_2-microglobulin, a serum protein, is unable to cross the dialysis filter and can aggregate into amyloid fibres which can deposit into joint spaces. Conventional thrice-weekly haemodialysis cannot clear the amount of β_2-microglobulin generated and it has been suggested that more frequent dialysis would reduce the plasma concentration of this molecule. It has been suggested that improved clearance of β_2-microglobulin is important for increased patient survival. The average rate of β_2-microglobulin removal was 15.59 ± 9.86 mg/ hour. Similarly, serum phosphate concentrations increase due to the dietary requirements placed on CKD patients. Phosphate is effectively removed with the average rate of removal of 69.56 ± 50.92 mg/ hour (Gura et al 2009a). The clearance rates of these so-called "middle molecules" appear to be more efficient with WAK than conventional haemodialysis probably due to differences in pump design,

[1] Carbon dioxide are released due to the decomposition of urea by urease in the sorbents cartridge

with the WAK pump providing simultaneous pulsatile flow of both blood and dialysate compared to the high amplitude and pulse frequency of the conventional roller pumps (Gura et al 2009b; Ronco et al 2008).

Table 2 Dialysis outcomes

		Mean ± SD
Treatment time		6.4 hrs ± 2.0
Blood flow (ml/min)		58.6 ± 11.7
Dialysate flow (ml/min)		47.1 ± 7.8
Weight (kg)	Before treatment After treatment	71.3 ± 23 70.5 ± 22.6, p = 0.01
Extracellular fluid/ total body fluid	Before treatment After treatment	0.339 ± 0.009 0.335 ± 0.010, p = 0.0019
Urea removed (mmol)		10.3 ± 4.8
Creatinine removed (mmol)		7.7 ± 4.4
Plasma urea clearance (ml/min)		22.7 ± 5.2
Plasma creatinine clearance (ml/min)		20.7 ± 4.8
Standard hourly urea clearance (Kt/V)		0.035 ± 0.01
β_2-microglobulin serum concentration before treatment		23.48 ± 4.44 mg/L 0.020 ± 0.004 mmol/L
Phosphate serum concentration before treatment		3.53 ± 2.48 mg/dL 1.14 ± 0.80 mmol/L
Inorganic phosphate removed (mg)		445.2 ± 325.9
β_2-microglobulin removed (mg)		99.8 ± 63.1
Inorganic phosphate clearance (ml/min)		21.7 ± 4.5
β_2-microglobulin clearance (ml/min)		11.3 ± 2.3

Kt/V quantifies haemodialysis treatment adequacy. K = urea clearance, t = dialysis time, V = patient's total body water

The same authors have reported on the development of the Vicenza wearable artificial kidney (ViWAK) for continuous peritoneal dialysis for CKD patients (Lee & Roberts 2008; Ronco et al 2008; Ronco & Fecondini 2007). To date, patient studies using the ViWAK have not commenced.

COST IMPACT

The authors of the included study were contacted for pricing information regarding the WAK device and consumables, however no response was received by the evaluators.

In Australia, using a steady-state projection model, it is estimated that the annual discounted cost of conventional, hospital-based RRT will increase from $560 million in 2004 to $605 million in 2010. However, if the number of CKD patients requiring

renal therapy increases as predicted, then this cost will increase to $697 million in 2010 (KHA 2006a). It has been estimated that each new dialysis patient costs the public hospital system approximately $65,000 a year.

The economic benefits in terms of reduced morbidity and mortality, in terms of hospital and patient resources, from increased rates of haemodialysis have not been determined.

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

OTHER ISSUES

No issues were identified/raised in the sources examined.

SUMMARY OF FINDINGS

Preliminary evidence of the wearable artificial kidney indicates that it is successful in the clearance harmful solutes and molecules that accumulate in patients with chronic kidney disease. The benefits of more frequent dialysis has been established and therefore a device which would enable patients to undergo dialysis frequently whilst able to participate in normal activities (including work) without being tied to a hospital setting would be advantageous both to the patient and to the health system. Studies where the WAK device is used long-term on a greater number of patients are required.

HEALTHPACT ACTION:

Based on the low-level, preliminary evidence the WAK device appears to be promising for the frequent treatment of chronic kidney disease patients. This device may have a great clinical impact in terms of reduced mortality and morbidity of CKD patients, and therefore may also represent savings in the health system. However this technology may be several years away from being a commercially viable proposition, therefore HealthPACT has recommended it be monitored for further information in 24-months time.

NUMBER OF INCLUDED STUDIES

Total number of studies	
Level IV intervention evidence	1

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SEARCH CRITERIA TO BE USED:

Chronic Disease
Creatinine/blood
Kidney Diseases
Kidney, Artificial
Kidney Failure, Chronic/*therapy
Renal Dialysis/*instrumentation/methods