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Australia and New Zealand Horizon Scanning Network

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Horizon scanning prioritising summary

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TherOx® AO system: hyperoxemic perfusion for myocardial infarction.

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PRIORITISING SUMMARY

REGISTER ID: **000142**

NAME OF TECHNOLOGY: **THEROX®AO SYSTEM**

PURPOSE AND TARGET GROUP: **HYPEROXEMIC PERFUSION FOR TREATMENT OF MICROVASCULAR ISCHAEMIA IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION**

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
United States	✓		
The Netherlands	✓		
Italy	✓		

IMPACT SUMMARY:

TherOx Inc. provides TherOx® aqueous oxygen (AO) System with the aim of treating and preventing damage to oxygen-deprived tissue. The system is approved for sale in Europe (personal communication, Therox Inc.). The TherOx® AO System is not available in Australia and is limited to investigational use in the United States.

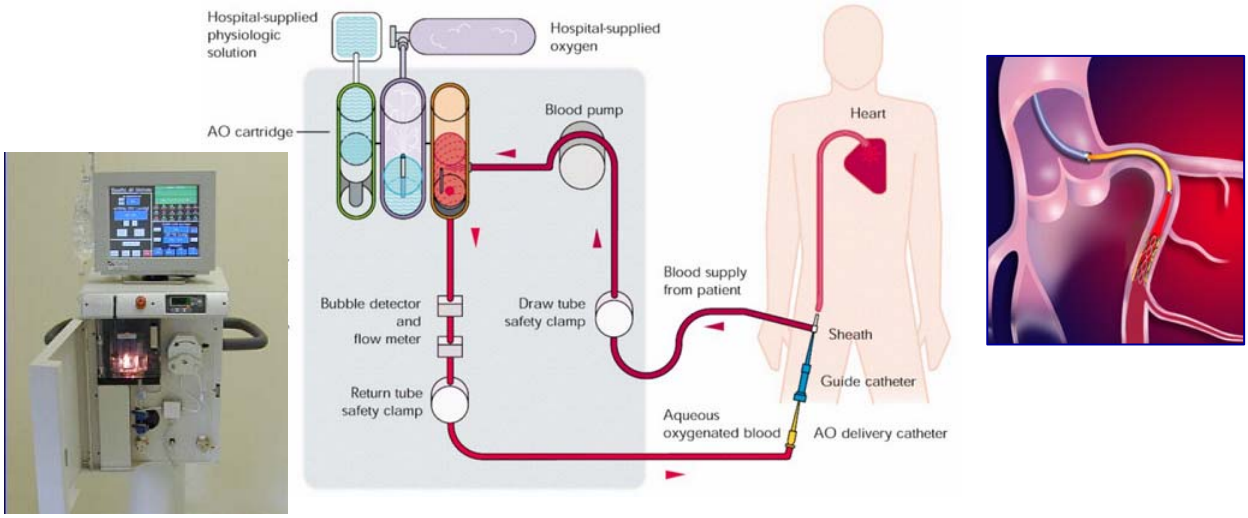
BACKGROUND

In patients with acute myocardial infarction (AMI), angioplasty is routinely performed to restore blood flow through the occluded coronary artery. However, successful reopening of blood vessel(s) does not necessarily lead to recovery of left ventricular function. It is common for patients post-AMI to experience a reduction in contractile function, which may result in heart failure. The reduced contractile function in the infarcted area is associated with poor microvascular perfusion, even after angioplasty has restored blood flow. The failure to re-establish adequate microvascular tissue perfusion may be due to ischemia-induced microvascular damage that occurs during the infarct (Bartorelli 2003). It has also been hypothesised that poor microvascular perfusion may also be caused by percutaneous coronary interventions such as angioplasty, as these procedures can create miniature wounds on vessel walls, which can trigger restenosis (Sharifi et al 2004).

The TherOx® AO System is a form of hyberbaric oxygen therapy. Hyperbaric oxygen therapy (HOT) is an established treatment for a range of indications including the treatment of severe burns, peripheral vascular disease and decompression. However, due to insufficient evidence the MSAC recommended that public funding should not be supported for the use of

hyperbaric oxygen therapy in the treatment of acute myocardial infarction (Villanueva et al 2001).

The aim of the TherOx® AO System is to treat damaged myocardial tissue arising from oxygen loss during or after AMI. The therapy is used as an adjunct to the initial interventions that restore blood flow to cardiac tissue. The treatment consists of withdrawing patients' blood and mixing with an aqueous oxygen solution, creating hyperoxemic blood and then re-infusing back to the tissue via a catheter for approximately 90 minutes. The infusion of the hyperoxygenated blood takes place via the same access point used during the initial angioplasty that restored blood flow, as illustrated below in figure 1.



TherOx® AO System device and components

Figure 1. Set-up and Delivery of TherOx® AO SystemTherapy (Printed with permission: Therox Inc)

The TherOx® AO System utilises two disposable components for each 90-minute treatment. The TherOx® AO Cartridge is a disposable, three-chambered cartridge installed into the AO system for the production of AO solution. The AO cartridge contains a sterile fluid path for connection to the patient arterial pathway via a specialised sub-selective AO delivery catheter. The AO delivery catheter is used for controlled, selective infusion of the AO-treated, hyperoxemic blood to the ischaemic region (TherOx Inc. 2005).

CLINICAL NEED AND BURDEN OF DISEASE

The number of angioplasty procedures performed in Australian hospitals in 2001-2 was 23,982, a rate of 122 per 100,000 (AIHW 2005a). In 2002-3 there were 43,767 hospital separations recorded for the principal diagnosis of Acute Myocardial Infarction (AIHW 2005b).

Myocardial infarction is a risk factor for heart failure. Heart failure as a principal diagnosis accounted for approximately 41,874 hospitalisations and 2,612 deaths in Australia during the period 2001-2002 (AIHW 2005c). The number of public hospital separations for patients with congestive heart disease or left ventricular failure was 28,113 and 12,648 respectively in 2001-2002 (AIHW 2005c).

DIFFUSION

The device is approved for investigational use in the United States and has been approved for use in Europe since 2002. As use of the TherOx® AO System has been limited, it is difficult to comment on the likely diffusion of the device in Australia. However, were the device found

to be effective as an adjunct to angioplasty in recovering myocardial function, and given there are no other existing treatments, it is likely to experience rapid uptake.

COMPARATORS
There are currently no other therapies available for recovering myocardial tissue damaged by AMI, however angioplasty may be offered to patients to prevent myocardial damage.

EFFECTIVENESS AND SAFETY ISSUES
See complete volume of Prioritising Summaries for definitions of Levels of Evidence.
The AMIHOT study (level II Intervention evidence) was conducted at 23 sites in the US and Europe. The aim of the study was to evaluate the safety of intra-coronary hyperoxemic therapy after angioplasty for AMI and to assess the effectiveness of hyperoxemic reperfusion to enhance recovery of left ventricular function. All of the 269 patients recruited to study were administered urgent angioplasty and were randomised to either angioplasty alone (135) or angioplasty with the TherOx® AO System (134).

The primary safety endpoint was the 30-day Major Adverse Coronary Events (MACE) measure, which is a composite of death, reinfarction, target vessel revascularisation (TVR) and stroke at 30 days. This study found hyperoxemic reperfusion with TherOx®AO was safe as an adjunct to angioplasty for AMI and there were no significant differences in MACE between the control and treatment groups.

The three primary effectiveness endpoints were ST segment resolution, infarct size at 14 days (assessed with single photon emission computed tomography imaging) and regional wall motion at three months. At three months there was no statistically significant difference between the groups with respect to infarct size or ST-segment resolution. There was also no significant difference in regional wall motion score between the control (n=119) and TherOx® (n=101) treatment group, (p=0.16).

This study went on to assess a subgroup of patients who had experienced an *anterior* acute myocardial infarction (76/119 and 80/101 patients in the control and treatment groups, respectively). A statistically significant improvement was reported in regional wall motion score (p=0.01) and ST-segment resolution (p =0.02) in patients treated with the TherOx® AO System compared to control patients within 6 hours of symptom onset (Martin et al 2004).

COST IMPACT
The system sells for $US35,000 and the disposable components cost $US2,000 per patient (personal communication TherOx Inc.).

Myocardial infarction is a risk factor for heart failure, which contributes significantly to Australian health system expenditure. A large proportion of health care expenditure (38%) is associated with hospitalising patients with heart failure (Mathers & Penm 1999).
A treatment to recover ischaemic tissue could result in a decrease in expenditure associated with the treatment and management of heart failure. Although it is possible that this treatment may only be suitable for a subgroup of these patients.

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.

CONCLUSION:
The TherOx® AO System aims at recovering/reversing myocardial damage from an AMI. Although it is not yet available for commercial use outside of Europe, there is potential for

this therapy to benefit a significant proportion of the Australian population. A subgroup analysis of a high level trial (level II evidence) indicated that this therapy may be safe and effective for patients with certain indications.

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

SOURCES OF FURTHER INFORMATION:

AIHW 2004. Heart, stroke and vascular diseases - Australian facts 2004. AIHW Cat. No. CVD 27. Canberra:

AIHW and National Heart Foundation of Australia (Cardiovascular Disease Series No. 22).

AIHW (2005a). '*Procedures Report for Cardiovascular Disease and Diabetes' National Cardiovascular Disease & Diabetes Database.*' [Internet]. Australian Institute of Health and Welfare. Available from: http://www.aihw.gov.au/pls/cvd/cvd_proc.show_report [Accessed 12th January, 2005].

AIHW (2005b). *'Principal diagnosis 0203' National Hospital Morbidity Database* [Internet]. Australian Institute of Health and Welfare. Available from: http://www.aihw.gov.au/cognos/cgi-in/ppdscgi.exe?DC=Q&E=/AHS/principaldiagnosis0203 [Accessed 12th January, 2005].

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Dixon, S. R.,Bartorelli, A. L.et al (2002). 'Initial experience with hyperoxemic reperfusion after primary angioplasty for acute myocardial infarction: results of a pilot study utilizing intracoronary aqueous oxygen therapy', *J Am Coll Cardiol*, 39 (3), 387-392.

Dixon R. 2004 'Final Results of the AMIHOT Trial of Post Reperfusion Supersaturated Oxygen Delivery' presentation at the Transcatheter Therapeutics Conference, Washington September 27 2004 – October 1 2004.

Martin, J.L., Lindsay, B.S. et al (2004). 'AMIHOT Phase II Clinical Study'presentation at the Transcatheter Therapeutics Conference, Washington September 27 2004 – October 1 2004.

Mathers C & Penm R 1999. Health system costs of cardiovascular diseases and diabetes in Australia 1993–94. Health and Welfare Expenditure Series No. 5. AIHW Cat. No. HWE 11.Canberra: AIHW.

Sharifi, M.,Fares, W.et al (2004). 'Usefulness of hyperbaric oxygen therapy to inhibit restenosis after percutaneous coronary intervention for acute myocardial infarction or unstable angina pectoris', *Am J Cardiol*, 93 (12), 1533-1535.

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TherOx Inc 2005. *'TherOx'* [Internet] Available from: http://www.therox.com/products.htm [Accessed 19th January, 2005].

Villanueva, E., Johnston, R. et al (2001). *Hyperbaric Oxygen Therapy*, Medical Services Advisory Committee, Canberra.

Zhdanov, G. G. & Sokolov, I. M. (2001). '[Tissue hypoxia in acute myocardial infarction and possible approaches to its correction]', *Anesteziol Reanimatol*, (3), 51-53.

SEARCH CRITERIA TO BE USED:
Coronary Angiography
Electrocardiography
Hyperbaric Oxygenation

Myocardial Infarction/physiopathology/radiography/ therapy
Myocardial Reperfusion
Oxygen/administration & dosage/metabolism/ therapeutic use