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Australia and New Zealand Horizon Scanning Network

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Horizon Scanning Technology Prioritising Summary

Implantable miniature telescope for macular degeneration

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PRIORITISING SUMMARY

REGISTER ID: **000192**

NAME OF TECHNOLOGY: **IMPLANTABLE MINIATURE TELESCOPE**

PURPOSE AND TARGET GROUP: **IMPLANTABLE TELESCOPE FOR THE TREATMENT OF AGE-RELATED MACULAR DEGENERATION**

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	✓		
Europe	✓		
South America	✓		

IMPACT SUMMARY:

This prioritising summary investigates the effectiveness of the Implantable Miniature Telescope, manufactured by VisionCare Ophthalmic Technologies, for the treatment of advanced age-related macular degeneration.

BACKGROUND

The Implantable Miniature Telescope (IMT) is designed to be a permanent solution for patients with advanced age-related macular degeneration (AMD). Advanced AMD is characterised by irreversible damage to the macula, or central retina, and an associated deterioration in central vision. Daily activities requiring detailed central vision, such as reading, watching television and recognising faces, become particularly difficult for people with advanced AMD. While central vision can be blurred or even missing, the peripheral vision of AMD patients generally remains intact. AMD can affect one or both eyes, and the disease can progress slowly or rapidly.

There are two distinct types of AMD, a dry or nonexudative form (geographic atrophy) and a wet or exudative form (neovascular). In the dry form of AMD, yellow deposits known as drusen form under the retina, interfering with the macula's cell metabolism and ability to process waste. In the early stage of dry AMD, often referred to as age-related maculopathy,

vision is generally unaffected and people are unlikely to know they have the condition. As the disease progresses however, the number of drusen under the retina increase and central vision slowly begins to deteriorate. Dry AMD can also progress to the more aggressive wet form of the disease. The wet form of AMD occurs when abnormal blood vessels develop behind the macula, the process often referred to as choroidal neovascularisation (CNV). The newly formed vessels are very fragile and can easily leak fluid and blood, leading to scar formation and permanent damage to the macula. Central vision can become distorted or entirely lost within a short period of time. Although the wet form of AMD is far less common than the dry form, it is responsible for the majority of cases of blindness or severe vision loss resulting from AMD (AIHW, 2005). Wet AMD has also been associated with increased depression, increased dependency and accidents, and an overall decrease in quality of life (Williams et al 1998; Tolman et al 2005).

Designed for patients with advanced dry and wet stage AMD, the IMT is a prosthetic telescope device measuring 4.4mm in length and weighing 46.1mg in an aqueous environment. The device is implanted behind the pupil in the posterior chamber of one eye during an outpatient surgical procedure that takes approximately 45 minutes. Once implanted, the IMT together with the cornea functions as a telephoto lens, providing three times magnification on the retina. The implanted eye provides central vision, while the non-implanted eye provides peripheral vision for orientation. A structured vision rehabilitation program is recommended for patients following surgery to help them adjust to the unequal images in the two eyes.

Clinical Need and Burden of Disease

In 2004, a total of 147,000 Australians over the age of 55 years were estimated to have advanced AMD, a prevalence rate among this group of 3.1 per cent. A further 491,900 Australians over the age of 55 years were estimated to have age-related maculopathy (early stage AMD), bringing the total number of older Australians affected by AMD to 638,900. Although the prevalence of advanced AMD in older Australians is not high relative to other diseases of the eye, it is easily the most common cause of blindness. In 2004, 56100 Australians over the age of 55 years were estimated to be blind, with AMD accounting for just over 50 per cent of this number (AIHW 2005).

The most significant risk factor for AMD is age. The disease rarely affects people under the age of 50, and incidence rates increase with age. In Australia in 2004, 67 per cent of patients with advanced AMD were 80 years of age or older (AIHW 2005). Other notable risk factors for AMD include family history, hypertension and smoking (Klein et al 2004; Mitchell et al 2002).

Diffusion

VisionCare Ophthalmic Technologies, the company responsible for developing and marketing the IMT, has just completed a phase II/III trial demonstrating the effectiveness of the device. At this stage however, the company has not received regulatory approval from the FDA to market the device.

Comparators

A variety of external visual aids are currently available to patients with advanced dry or wet stage AMD, including high plus lenses and external telescopes. Similar to the IMT, these devices use magnification to increase the size of the image on the retina. High plus lenses have the disadvantage of a very short focal length, making them inappropriate for a large number of visual tasks. External telescopes are generally cumbersome and cosmetically unappealing, and the visual field they offer is severely restricted (5 to 10 degrees, compared to 36 degrees for the IMT). Patients can also experience nausea when using external

telescopes because of the vestibular ocular reflex conflict caused by the need to scan the visual field using head movement rather than natural eye movement (Peli 2002).

A number of non-optical treatments for AMD have also been developed. Photodynamic therapy, approved by the FDA in 2000, has shown success in preventing further deterioration of vision in patients with wet AMD. Unfortunately the treatment is expensive, difficult to access and is only appropriate for patients with early stage wet AMD. In 2004, the FDA approved Macugen (pegaptanib sodium injection) for the treatment of early stage wet AMD. Macugen is a vascular endothelial growth factor inhibitor that attacks the vascular growth and leakage responsible for vision loss in wet AMD. While Macugen may be effective in preventing further vision loss, it has not been shown to improve visual acuity in patients. Furthermore, it only has a short-term effect and must be re-administered every six weeks.

EFFECTIVENESS AND SAFETY ISSUES

An early phase I study by Lane et al (2004) (level IV intervention evidence) evaluated the safety and effectiveness of the IMT in a group of 13 patients with advanced dry and wet stage AMD. All patients were 60 years of age or older (mean age 80 years), with best-corrected visual acuity (BCVA) between 20/80 and 20/400 in both eyes. At 12 months, ten of the 13 patients who underwent surgery gained two or more lines of either distance or near BCVA, while eight of 13 gained three or more lines. Mean endothelial cell density decreased by 13 per cent after 12 months, indicating that the corneal endothelium tolerated the procedure well. Finally, all adverse events in the study were resolved with appropriate corticosteroid treatment.

In a similar study, Alió et al (2004) (level IV intervention evidence) assessed the safety and effectiveness of the IMT in 40 patients suffering from advanced dry stage AMD. In the study, patients were 60 years or older (mean age 77.1 years), with BCVA in the implanted eye between 20/80 and 20/200, and BCVA in the fellow eye of 20/80 or worse. In the operated eye, mean uncorrected visual acuity (UCVA) from a distance improved from 0.9 logMAR (minimum angle of resolution) prior to the operation to 0.6 logMAR 12 months later ($p<0.001$). Similarly, near UCVA in the operated eye improved from 0.8 logMAR prior to operation to 0.4 logMAR one year later ($p=0.01$). Few complications were reported during the course of the study. Seven patients developed persistent complications in the form of persistent capsular opacification (n=4), synechias (n=2) and fibrin deposition on the pupil (n=1).

VisionCare Ophthalmic Technologies recently released twelve month results of their multicentre study (level IV intervention evidence) in which the IMT was implanted in 206 patients with advanced dry and wet stage AMD (VisionCare, 2006). In the study, patients had a mean age of 76 years and reported moderate to severe levels of visual impairment prior to implantation, with BCVA ranging between 20/80 and 20/800 in both eyes. Twelve months after IMT implantation, patients demonstrated a mean improvement in the study eye of over three lines in both distance and near BCVA. Preservation of vision was achieved in 95 per cent of patients (exceeding the protocol-specified target of 90 per cent). Significant improvements in vision related quality of life were also reported. Patients improved significantly from baseline (range 7-14 points, $p<0.01$) in seven of eight vision-specific and psychosocial subscales of the National Eye Institute Visual Function Questionnaire. Finally, mean endothelial cell density had decreased by 25 per cent at 12 months (protocol-specified target 17 per cent). Although two-year safety surveillance is now complete, results are yet to be published.

COST IMPACT

The specific cost of the IMT is yet to be determined. In addition to the device itself, the implantation procedure and associated rehabilitation would attract further costs. The

implantation of the IMT is performed under local anaesthetic in an outpatient cataract surgery procedure that takes approximately 45 minutes. Following surgery, patients are encouraged to see a rehabilitation specialist for at least a month to help them adjust to the unequal images in the two eyes.

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.

RECOMMENDATION:

AMD is the leading cause of blindness amongst older Australians. Patients affected by AMD, particularly its wet form, often experience difficulties performing daily activities that require detailed central vision. AMD has been associated with increased depression, increased dependency, and an overall decrease in quality of life. Given the extensive burden of the disease and the lack of current treatment alternatives, the IMT offers significant health benefits for patients with advanced AMD. The case series results reported by VisionCare Ophthalmic Technologies provide limited evidence for the effectiveness of the IMT, however questions remain regarding the long-term safety of the device, its overall cost impact and the timeliness of its availability in Australia. It is recommended therefore that the following be conducted:

☐	Horizon Scanning Report	☐	Full Health Technology Assessment
☒	Monitor	☐	Archive

SOURCES OF FURTHER INFORMATION:

AIHW (2005). *Vision problems among older Australians,* Australian Institute of Health and Welfare, Canberra.

Alio, J. L., Mulet, E. M. et al (2004). 'Intraocular telescopic lens evaluation in patients with age-related macular degeneration', *J Cataract Refract Surg,* 30 (6), 1177-1189.

Klein, R., Peto, T. et al (2004). 'The epidemiology of age-related macular degeneration', *Am J Ophthalmol,* 137 (3), 486-495.

Lane, S. S. & Kuppermann, B. D. (2006). 'The Implantable Miniature Telescope for macular degeneration', *Curr Opin Ophthalmol,* 17 (1), 94-98.

Lane, S. S., Kuppermann, B. D. et al (2004). 'A prospective multicenter clinical trial to evaluate the safety and effectiveness of the implantable miniature telescope', *Am J Ophthalmol,* 137 (6), 993-1001.

Mitchell, P., Wang, J. J. et al (2002). 'Smoking and the 5-year incidence of age-related maculopathy: the Blue Mountains Eye Study', *Arch Ophthalmol,* 120 (10), 1357-1363.

Peli, E. (2002). 'The optical functional advantages of an intraocular low-vision telescope', *Optom Vis Sci,* 79 (4), 225-233.

Tolman, J., Hill, R. D. et al (2005). 'Psychosocial adaptation to visual impairment and its relationship to depressive affect in older adults with age-related macular degeneration', *Gerontologist,* 45 (6), 747-753.

VisionCare (2005). [Internet]. Available from: http://www.visioncareinc.net/2005_10_19.html [Accessed 21st March 2006].

Williams, R. A., Brody, B. L. et al (1998). 'The psychosocial impact of macular degeneration', *Arch Ophthalmol,* 116 (4), 514-520.

LIST OF STUDIES INCLUDED

Total number of studies

Level IV evidence 3

SEARCH CRITERIA TO BE USED:

Macular Degeneration/diagnosis/*rehabilitation
Lens Implantation, Intraocular/*methods
Macular Degeneration
Visual Fields
Blindness/etiology/psychology

HEALTH PACT DECISION:

- ☐ Horizon Scanning Report
- ☐ Full Health Technology Assessment
- ☐ Monitor
- ☐ Archive
- ☐ Refer

PRIORITY RATING

- ☐ **High**
- ☐ **Medium**
- ☐ **Low**

APPENDIX

20/20 vision is a term used to describe normal distance vision. The '20' represents a distance of 20 feet, the standard testing distance used by optometrists. In metric countries such as Australia vision may be described as 6/6, where the six represents 6 metres. If an individual is described as having 20/40 vision, then that person must stand at 20 feet to see what a person with normal vision can see at 40 feet. 20/200 vision is the cut off for legal blindness. Conversely, an individual with 20/10 vision has above normal vision (Optometrist Australia, 2003).

AUGUST 2007 UPDATE

AUGUST 2007 COMPARATORS:

A pilot study involving 35 subjects reported that an intraocular implant consisting of two lenses, which when installed form an effective telescope, improved visual acuity of all subjects (level IV intervention evidence). Some subjects had both eyes implanted giving a total of 40 eyes treated. The mean post-operative best corrected visual acuity of subjects was 0.77 (the logarithm of the minimum angle of resolution) compared to the pre-operative mean of 1.28. Other measures of visual improvement also increased including a gain of 6.2 times best reading magnification and the mean post-operative reading distance gain was 7.66 cm. No complications were detected in the study (Orzalesi et al 2007).

AUGUST 2007 SAFETY AND EFFECTIVENESS ISSUES:

During the preparation of the prioritising summary information regarding a preliminary report of unpublished results was found on the Visioncare website. Since the publication of the prioritising summary the full results have been published in the peer reviewed journal Opthamology (Hudson et al 2006)(level IV intervention evidence). Additional information presented in the full publication will be summarised here. As reported previously the treated eyes showed improvement over 12 months post-operation. In addition, it is now reported that the untreated companion eyes continued to degenerate significantly over the same follow-up period. Improvements in quality of life were noted in the preliminary report but the nature of these improvements were not described or quantified. It is now reported that the National Eye Institute 25-item Visual Function questionnaire (NEI VFQ-25) scores improved significantly (6.1 ±14.4 points: p <0.0001) over the baseline scores. There was no significant association between NEI VFQ-25 scores and device model. Other significant changes were positive increases in social functioning, mental health, and lower dependency. Ocular pain did not change significantly and peripheral vision decreased significantly, the decrease in peripheral vision was a known factor resulting from the design of the IMT. It was also stated that out of the original 217 patients who were enrolled for surgical implant, 11 underwent single lens implantation due to aborted IMT implantation.

In the 109th meeting of the FDA Opthalmic Devices Panel evidence concerning the IMT was presented by patients, surgeons who fitted the device, VisionCare, and the FDA itself. At this presentation it was noted that the subjects involved in the trial had consented to five years of follow up after the initial installation of the device. As mentioned above there were originally 217 patients enrolled to have the device implanted, the complications that caused the withdrawal of 11 patients were: seven cases of posterior capsular rupture, two eyes identified as having choroidal detachment, one eye with choroidal hemorrhage, and one eye with loss of zonular support.

The trial goals were an improvement in near or far vision of two lines or more at twelve months post installation. Nearly 90 percent of subjects achieved this at 12 months and this figure was not altered at 24 months post installation. More than two lines of best corrected visual acuity (BCVA) were lost in 2.5 percent of eyes. Eight devices were removed due to device failure (n=2), patient requests due to unsatisfactory results (n=4) and two cases of corneal decompensation. The device was found to have not contributed to falls that the elderly subjects experienced during the trial period. A concern for the long term safety of the device is the loss of endothelial cell density (ECD) of the eye. Up to the time of the FDA meeting the ECD loss resulting from IMT was not statistically different to than for typical cataract surgery. The FDA reviewers used a model to predict the future ECD losses. This model predicted that, at 24 months, no fellow untreated eyes would reach 20 per cent ECD loss, yet nine per cent of IMT treated eyes would have greater than 50 per cent ECD loss.

At an ECD of below 500 per mm^2 corneal decompensation can occur. Given the subjects started with ECD 1600 per mm^2 loss at this predicted rate could be clinically significant. The FDA panel agreed that the trial failed to meet the safety goal of ECD loss being less ≤ 17 per cent, in fact the mean loss was 25.3 per cent. Another significant issue raised was the anterior chamber depth of the subject's eye. With low ACD there was a greater chance of serious complications and this was reflected in the initial trial data where smaller ACD subjects had more complications. The FDA voted against the approval of the IMT citing lack of effectiveness and safety data, particularly the ECD loss levels were above what was considered safe and the data for those patients who had adverse effects was lacking (FDA 2006).

AUGUST 2007 OTHER ISSUES:

A case report of an 81 year old patient undergoing thermal laser photocoagulation of a choroidal neovasacular membrane through an implanted IMT showed it was possible to successfully perform procedures with the IMT in place. The IMT was not damaged in the process and three months after laser treatment no recurrence of the original symptoms were noted (Garfinkel et al 2006).

AUGUST 2007 COST IMPACT :

No information was found regarding cost impact in the evidence reviewed in this summary.

AUGUST 2007 SUMMARY OF FINDINGS:

The IMT device gave patients a significant improvement in their vision as reported to the FDA. But despite this there were serious safety concerns and a lack of data for the patients who did not benefit from the device implantation. Further evidence is required to fully assess whether the IMT will be a device worthy of clinical use.

AUGUST 2007 HEALTHPACT ACTION:

Given that this device currently does not have regulatory approval from the TGA, HealthPACT have recommended that further assessment is no longer warranted.

NUMBER OF STUDIES INCLUDED

Total number of studies	1
Level IV evidence	1

AUGUST 2007: REFERENCES:

FDA (2006). *Ophthalmic devices panel of the Medical Devices Advisory Committee,* U.S. Food and Drug Administration. http://www.fda.gov/OHRMS/DOCKETS/AC/06/transcripts/2006-4225t.pdf

Garfinkel, R. A., Berinstein, D. M. & Frantz, R. (2006). 'Treatment of choroidal neovascularization through the implantable miniature telescope', *Am J Ophthalmol,* 141 (4), 766-767.

Hudson, H. L., Lane, S. S. et al (2006). 'Implantable miniature telescope for the treatment of visual acuity loss resulting from end-stage age-related macular degeneration: 1-year results', *Ophthalmology,* 113 (11), 1987-2001.

Orzalesi, N., Pierrottet, C. O. et al (2007). 'The IOL-Vip System: a double intraocular lens implant for visual rehabilitation of patients with macular disease', *Ophthalmology,* 114 (5), 860-865.

AUGUST 2007 SOURCES OF FURTHER INFORMATION:

No other sources were identified.