

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

### Interventional procedure consultation document

# Insertion of a subretinal prosthesis system for retinitis pigmentosa

Retinitis pigmentosa is a disease that affects light-sensitive cells in the back layer of the eye (retina), typically leading to progressive loss of vision and sometimes blindness. In this procedure a light-sensitive microchip is implanted behind the retina to take on the function of damaged cells and help the person to see basic images.

The National Institute for Health and Care Excellence (NICE) is examining insertion of a subretinal prosthesis system for retinitis pigmentosa and will publish guidance on its safety and efficacy to the NHS. NICE's Interventional Procedures Advisory Committee has considered the available evidence and the views of specialist advisers, who are consultants with knowledge of the procedure. The Advisory Committee has made provisional recommendations about insertion of a subretinal prosthesis system for retinitis pigmentosa.

This document summarises the procedure and sets out the provisional recommendations made by the Advisory Committee. It has been prepared for public consultation. The Advisory Committee particularly welcomes:

- comments on the provisional recommendations
- the identification of factual inaccuracies
- additional relevant evidence, with bibliographic references where possible.

**Note that this document is not NICE's formal guidance on this procedure. The recommendations are provisional and may change after consultation.**

The process that NICE will follow after the consultation period ends is as follows.

- The Advisory Committee will meet again to consider the original evidence and its provisional recommendations in the light of the comments received during consultation.

- The Advisory Committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.

For further details, see the [Interventional Procedures Programme process guide](#), which is available from the NICE website.

Through its guidance NICE is committed to promoting race and disability equality, equality between men and women, and to eliminating all forms of discrimination. One of the ways we do this is by trying to involve as wide a range of people and interest groups as possible in the development of our interventional procedures guidance. In particular, we aim to encourage people and organisations from groups who might not normally comment on our guidance to do so.

In order to help us promote equality through our guidance, we should be grateful if you would consider the following question:

Are there any issues that require special attention in light of NICE's duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations between people with a characteristic protected by the equalities legislation and others?

Please note that NICE reserves the right to summarise and edit comments received during consultations or not to publish them at all where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would otherwise be inappropriate.

Closing date for comments: 6th August 2015

Target date for publication of guidance: September 2015

## **1 Provisional recommendations**

- 1.1 Current evidence on the safety and efficacy of insertion of a subretinal prosthesis system for retinitis pigmentosa is limited in quality and quantity. Therefore, this procedure should only be used in the context of research.
- 1.2 NICE encourages further research on this procedure. Outcomes should include the impact on quality of life and activities of day-to-day living, and durability of implants. NICE may update the guidance on publication of further evidence.

## **2 Indications and current treatments**

- 2.1 Retinitis pigmentosa is the encompassing term for a group of degenerative eye conditions that cause progressive loss of retinal photoreceptors. The disease is often inherited. Patients initially experience ring scotoma and night vision problems which, in most cases, slowly progress and lead to the loss of all peripheral vision. Central vision is usually preserved until late stages of the disease, but can be lost earlier with severe disease.
- 2.2 Conservative treatments are aimed at early identification and treatment of complications such as cataract or macular oedema. Some newer treatments aim to slow the progression of the condition. Surgical treatments are being developed, including epiretinal and subretinal prostheses, as well as optic nerve implants to restore basic sight.

## **3 The procedure**

- 3.1 Retinitis pigmentosa causes loss of retinal photoreceptors but inner retinal cells (ganglion and bipolar cells) remain intact. Subretinal prosthesis systems aim to restore perception of light, movement, and shapes by surgically implanting a microchip behind the retina. The microchip mimics the function of damaged outer retinal photoreceptors by absorbing light and converting it into retinotopically correct electrical pulses that stimulate the overlying bipolar cell layer. The bipolar cells propagate the signal to downstream retinal cells, which send visual information to the brain.
- 3.2 Implantation of the microchip is done with the patient under general anaesthesia. A vitrectomy is performed and the microchip is implanted underneath the macula using a transscleral, then

subretinal approach. The microchip connects to a thin cable that exits the eye at the equator, through the choroid and sclera, and runs under the skin to a power source which is fixed to bone in the retroauricular region. This, in turn, connects to an external power source/control unit via a removable, surface mounted induction loop.

## 4 Efficacy

This section describes efficacy outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#) *[add URL]*.

- 4.1 In a case series of 6 patients, improvements in visual acuity (measured by the smallest Early Treatment of Diabetic Retinopathy study [ETDRS] letters that could be read) were reported in 3 patients. Visual acuity improved in 1 patient from a Snellen equivalent of 20/800 before the procedure to 20/200 at 6 month follow-up. In the second patient, visual acuity improved from 20/1600 before the procedure to 20/400 at 6 month follow-up. The third patient had been unable to read ETDRS letters before the procedure but had a visual acuity of 20/1600 at 18 month follow-up.
- 4.2 In a case series of 9 patients, light perception thresholds were considerably better when prosthesis systems were switched on compared against when they were switched off. All patients were able to perceive light when their prosthesis systems were switched on, at maximum follow-up of 9 months. No further details were provided.

- 4.3 In the case series of 9 patients, patients were asked to indicate the direction (up, down, left or right) of the pointed end of a white wedge on a black screen. Seven patients correctly indicated the direction in which the wedge was pointing when their prosthesis systems were switched on, at maximum follow-up of 9 months.
- 4.4 In the case series of 9 patients, patients were asked to count, locate and identify 4 of 6 possible geometric shapes that were placed on a black table cloth. The mean number of shapes counted was 2.8 when prosthesis systems were switched on, compared against 0.5 when prosthesis systems were switched off, at maximum follow-up of 9 months ( $p=0.012$ ). The mean number of shapes located was 2.2 when prosthesis systems were switched on, compared against 0.5 when prosthesis systems were switched off ( $p=0.012$ ). The mean number of shapes correctly identified was 1 when prosthesis systems were switched on, compared against 0.1 when prosthesis systems were switched off ( $p=0.018$ ).
- 4.5 Specialist advisers listed key efficacy outcomes as improvement of visual function (recognition and discrimination of words or objects, as well as perception of light, movement or direction), performance in spatial or motor tasks (including activities of daily living), and improved quality of life.

## 5 Safety

This section describes safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#) [add URL].

- 5.1 In a case series of 9 patients, 75 adverse events occurred within 1 year of prosthesis implantation. These included:
- 'retinal break' without detachment – 2 cases (3% of adverse events): neither resolved (no further details provided)
  - Conjunctival erosions above the external part of the cable and/or suture erosions through the conjunctiva – 12 cases (16% of adverse events): all resolved without sequelae (no further details provided)
  - conjunctival hyperaemia – 6 cases (8% of adverse events): all resolved without sequelae (no further details provided)
  - retinal vascular leakage and neovascularisation – 10 cases (13% of adverse events): 2 occurred before device implantation. Nine did not resolve. In 1 patient, retinal vascular leakage resulted in damage to eye structures and loss of light perception
  - retinal haemorrhage – 7 cases (9% of adverse events): all resolved without sequelae (no further details provided)
  - ocular hypertension – 8 cases (11% of adverse events): all resolved without sequelae (no further details provided)
  - paraesthesia of the skin (location not specified) – 3 cases (4% of adverse events): all resolved without sequelae (no further details provided)
  - epistaxis – 2 cases (3% of adverse events): both resolved without sequelae (no further details provided).
- 5.2 In the case series of 9 patients a single occurrence of each of the following was reported within 1 year of prosthesis implantation: intraoperative perforation of the choroid, intraoperative contact of the optic nerve head with the implant, postoperative bleeding, contusion of the eyelid and periocular area, mucopurulent

conjunctivitis, a peripheral corneal dent, acute iritis, retinal detachment with a retinal break, ocular pain, dizziness, headache, and chronic pain (unspecified location). Intraoperative perforation of the choroid and intraoperative contact of the optic nerve head with the implant both occurred in the same patient and resulted in loss of residual vision in the study eye. All other adverse events resolved without sequelae.

5.3 Aniseikonia was reported in 1 patient in a case series of 6 patients (the timing of occurrence was not reported). This was treated by implantation of an anterior chamber intraocular lens.

5.4 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers listed the following anecdotal adverse events: minor intraoperative subretinal bleeding, and the implant malfunctioning, requiring removal and replacement. They considered that the following were theoretical adverse events: intraocular haemorrhage, glaucoma, photopsia, choroidal neovascularisation, thermal injury to neurons, choroidal or retinal circulation abnormalities, and complications associated with vitrectomy.

## **6 Committee comments**

6.1 The Committee noted that insertion of a subretinal prosthesis system for retinitis pigmentosa is intended for patients with end-stage disease who have no useful sight and no other treatment options. It recognised that even minor improvements in vision may help these patients, but it wanted evidence that any changes in

metrics of vision result in improvements in quality of life and activities of daily living. These considerations underpinned the specific recommendations about research in section 1.2.

- 6.2 The Committee recognised that the technology of subretinal prostheses and related devices is evolving and that further developments may result in substantial changes to outcomes which may influence patient selection in the future.
- 6.3 The Committee noted the importance of careful patient selection, including psychological counselling to ensure that patients have realistic expectations. It also noted the need for continued expert care of patients and their subretinal prostheses after the procedure.

## **7 Further information**

- 7.1 For related NICE guidance, see the [NICE website](#).

Bruce Campbell

Chairman, Interventional Procedures Advisory Committee

May, 2015