

Photodynamic therapy for high-grade dysplasia in Barrett's oesophagus

1 Guidance

- 1.1 Current evidence on the safety of photodynamic therapy for high-grade dysplasia in Barrett's oesophagus appears adequate to support the use of this procedure. Photodynamic therapy appears efficacious in downgrading dysplasia in Barrett's oesophagus, when used for the treatment of high-grade dysplasia (a pre-malignant lesion). However, its efficacy in preventing the progression of Barrett's oesophagus to invasive cancer is not clear.
- 1.2 Clinicians wishing to undertake photodynamic therapy for high-grade dysplasia in Barrett's oesophagus should take the following actions.
 - Inform the clinical governance leads in their Trusts.
 - Inform patients, as part of the consent process, about the uncertainty of influencing their long-term prognosis and provide them with clear written information. Use of the Institute's *Information for the Public* is recommended.
 - Audit and review clinical outcomes of all patients having photodynamic therapy for high-grade dysplasia in Barrett's oesophagus.
- 1.3 Publication of long-term efficacy outcomes will be useful in reducing the current uncertainty. Randomised trials are in progress and clinicians are encouraged to consider entering patients into these (www.cancerhelp.org.uk/trials/trials/default.asp). The Institute may review the procedure upon publication of further evidence.
- 1.4 This guidance is limited to the procedure using pharmaceuticals licensed for photodynamic therapy of oesophageal dysplasia.

2 The procedure

2.1 Indications

- 2.1.1 Barrett's oesophagus is a condition characterised by an abnormal lining of the oesophagus, which occurs in patients with a long history of gastro-oesophageal reflux disease.
- 2.1.2 In a minority of people, Barrett's oesophagus may progress through a series of increasingly severe stages (dysplasia) to cancer. High-grade dysplasia is the stage that immediately precedes the occurrence of cancer, but it is not possible to predict how soon cancer will develop. The grade of dysplasia and the amount of oesophagus affected are thought to be the most important risk factors for progression to cancer.
- 2.1.3 Oesophagectomy is the most radical treatment option for high-grade dysplasia, because removal of the whole oesophagus means that the risk of progression to cancer is removed. However, oesophagectomy is a major operation with the potential for morbidity and mortality. Less invasive treatments include laser ablation, endoscopic mucosal resection and photodynamic therapy. All of these procedures aim to ablate the specialised columnar epithelium that is affected by dysplasia and to promote the regeneration of normal squamous epithelium.

2.2 Outline of the procedure

- 2.2.1 Photodynamic therapy involves the administration of a photosensitising agent. The agent is then activated by the application of light to the selected area, usually with a low-power laser. It absorbs the energy from the light, resulting in the formation of high-energy oxygen molecules. These molecules interact with

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This guidance is written in the following context:

This guidance represents the view of the Institute which was arrived at after careful consideration of the available evidence. Health professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of health professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

the tissue, leading to necrosis by a photochemical rather than a thermal effect. A variety of photosensitising agents are in the process of research and development.

- 2.2.2 Treatment can be performed on an outpatient basis and is usually applied to approximately 7 cm of the affected oesophagus at one time, to avoid toxicity. A second treatment session may be conducted if the affected area is larger than 7 cm.

2.3 Efficacy

- 2.3.1 The evidence on efficacy is based largely on three uncontrolled reports and one unpublished randomised trial. The results of all four reports showed that dysplasia was downgraded (from high-grade dysplasia to Barrett's oesophagus without dysplasia) in the majority of patients (77–98%) following the procedure. Elimination of Barrett's oesophagus was achieved in 42% (25/60) to 98% (47/48) of patients; however, residual disease was often ablated by laser treatment. For more details, refer to the Sources of evidence (see below right).
- 2.3.2 In a study of 80 patients with high-grade dysplasia, in which 65 patients were followed up for a mean of 58 months, 3 developed carcinoma. Initial results from the unpublished randomised controlled trial indicate that at 24 months, 14% (18/130) of patients treated with photodynamic therapy progressed to cancer, compared with 29% (20/70) of patients receiving medication only. This study is still in progress and these are preliminary findings only. For more details, refer to the Sources of evidence.
- 2.3.3 One Specialist Advisor stated that a proportion of patients undergoing photodynamic therapy may have an undetected invasive carcinoma, which would be beyond the reach of the therapy.

2.4 Safety

- 2.4.1 Oesophageal strictures and cutaneous reactions associated with the photosensitiser were the most commonly reported complications following photodynamic therapy. Oesophageal strictures occurred in 23% (11/48) to 34%

(34/100) of patients in the published studies. Skin reactions occurred in around one third of patients undergoing photodynamic therapy. These included mild, moderate and severe reactions, with 3% (3/100) to 15% (7/48) of patients experiencing severe photosensitivity reactions requiring medical treatment. For more details, refer to the Sources of evidence (see below).

- 2.4.2 Oesophageal perforation, pleural effusions and atrial fibrillation were also reported, with an incidence of around 3–4%. For more details, refer to the Sources of evidence.
- 2.4.3 The Specialist Advisors listed the main adverse events as photosensitivity and development of strictures. One Advisor stated that underlying malignancy might continue to grow unobserved because of the superficial healing of the Barrett's oesophagus. One Advisor noted pleural effusions and atrial fibrillation as potential complications.

2.5 Other comments

- 2.5. The current evidence is based on small patient numbers.

Andrew Dillon
Chief Executive
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Information for the Public

The Institute has produced information describing its guidance on this procedure for patients, carers and those with a wider interest in healthcare. It explains the nature of the procedure and the decision made, and has been written with patient consent in mind. This information is available, in English and Welsh, from www.nice.org.uk/IPG082publicinfo

Sources of evidence

The evidence considered by the Interventional Procedures Advisory Committee is described in the following document.

Interventional procedure overview of photodynamic therapy for high-grade dysplasia in Barrett's oesophagus, November 2003

Available from: www.nice.org.uk/ip232overview

Ordering information

Copies of this guidance can be obtained from the NHS Response Line by telephoning 0870 1555 455 and quoting reference number N0668. *Information for the Public* can be obtained by quoting reference number N0669 for the English version and N0670 for a version in English and Welsh.

The distribution list for this guidance is available on the NICE website at URL www.nice.org.uk/IPG082distributionlist

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