Assessment of photodynamic therapy using porfimer sodium for esophageal, bladder and lung cancers

SUMMARY

AGENCE D'ÉVALUATION DES TECHNOLOGIES
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Québec

Assessment of photodynamic therapy using porfimer sodium for esophageal, bladder and lung cancers

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Report prepared for AETMIS
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MISSION

The mission of the *Agence d'évaluation des technologies et des modes d'intervention en santé* (AETMIS) is to contribute to improving the Québec health-care system and to participate in the implementation of the Québec government's scientific policy. To accomplish this, the Agency advises and supports the Minister of Health and Social Services as well as the decision-makers in the health-care system, in matters concerning the assessment of health services and technologies. The Agency makes recommendations based on scientific reports assessing the introduction, diffusion and use of health technologies, including technical aids for disabled persons, as well as the modes of providing and organizing services. The assessments take into account many factors, such as efficacy, safety and efficiency, as well as ethical, social, organizational and economic implications.

FOREWORD

ASSESSMENT OF PHOTODYNAMIC THERAPY USING PORFIMER SODIUM FOR ESOPHAGEAL, BLADDER AND LUNG CANCERS

Cancer, in all its forms, contributes significantly to morbidity and mortality in the Québec population. It continues to be a priority target for action, not only for health policies and health-care programs but also for research. For clinicians, accessing the best techniques for destroying cancer cells and thereby ensuring their patients' survival while minimizing any adverse effects, is a constant challenge. These techniques also alleviate symptoms and ensure the best quality of life possible when progression of cancer cannot be controlled.

Such is the context surrounding the assessment of photodynamic therapy using porfimer sodium. Porfimer sodium is a photosensitizing agent approved in Canada in 1993 for three oncological indications: lung, bladder and esophageal cancers. More recently, it has also been approved for the treatment of Barrett's esophagus with dysplasia, a major risk factor in esophageal cancer.

Given that the effectiveness of this new non-invasive technology has not yet been fully demonstrated, the *Ministère de la Santé et des Services sociaux* (MSSS) asked the *Agence d'évaluation des technologies et des modes d'intervention en santé* (AETMIS) to examine its efficacy and its potential impact on the health network. Following standard procedure, AETMIS first reviewed the scientific literature available and then made recommendations on the introduction and management of this technology.

In conclusion, photodynamic therapy remains a promising treatment whose evolution must continue to be monitored, especially with respect to the photosensitizing agents themselves. Currently, proven indications are limited to the palliative treatment of advanced esophageal cancer, and it is difficult to estimate the relative importance of this technology in the therapeutic arsenal available for the other oncological applications. A more in-depth examination should be conducted on potential use of this technology in the treatment of Barrett's esophagus with dysplasia. In such case, the use of this therapy would affect a greater number of patients since this disorder may appear after gastric reflux, a very widespread problem today.

In submitting this report, AETMIS hopes to contribute to ensuring the best possible use of the different oncology resources available for the benefit of all patients with cancer.

Renaldo N. Battista
President

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Note that Dr. Jacques Jolivet was the external reviewer designated by the *Conseil québécois de lutte contre le cancer* (CQLC), an agency that works in close partnership with AETMIS in all oncology-related matters. We wish to thank the CQLC and its president, Dr. Jean Latreille, for their collaboration.

SUMMARY

DESCRIPTION OF THE TECHNOLOGY

Photodynamic therapy (PDT) is used to treat several types of cancer. It consists in marking pathological tissue with a photosensitizing agent and then selectively destroying the tissue by exposing it to a light source with a specific wavelength. This monochromatic light is normally produced by a laser or a laser diode. In general, the photosensitizing agent is systemically administered to all body cells but is preferentially retained by pathological cells.

Hematoporphyrin derivatives are used as photosensitizing agents. Approved by Canada in April 1993 for three oncological indications (lung, bladder and esophageal cancers), porfimer sodium (Photofrin®) is the most widely used agent in photodynamic therapy. More recently, this product has also been approved for the treatment of Barrett's esophagus with dysplasia. This disorder appears after gastric reflux and is a major risk factor in esophageal cancer.

Porfimer sodium is activated by a light of 630 nm, but penetration is poor at that wavelength, a serious handicap when tumours are larger and deeper. This agent has a further limitation—skin photosensitivity persisting for up to six weeks after treatment. For that reason, several research projects are striving to develop agents that do not present the disadvantages and limitations of porfimer sodium. Finally, determining the appropriate dosimetry, for both the photosensitizer and the light source, is a continual challenge and remains under investigation.

ORIGIN AND OBJECTIVES OF THE ASSESSMENT

The *Ministère de la Santé et des Services sociaux* (MSSS) asked the *Agence d'évaluation des technologies et des modes d'intervention en santé* (AETMIS) to evaluate the efficacy of photodynamic therapy using porfimer sodium for its approved oncological indications. This report reveals the results of the assessment, attempts to adequately situate this treatment within the therapeutic arsenal available in Québec, and presents some preliminary observations on its use for the treatment of Barrett's esophagus.

METHODOLOGY

The literature search strategy we used located two reports produced by health-technology assessment agencies: the *Comité d'évaluation et de diffusion des innovations technologiques* (CEDIT), associated with the *Assistance Publique–Hôpitaux de Paris*, in France (1999), and the Institute for Clinical Systems Improvement (ICSI) in the United States (1997 and 2002). To supplement this information, we searched MEDLINE for all relevant articles published between January 1997 and December 2003. Assessment of these studies was based on the scheme for grading scientific evidence proposed in the *Canadian Guide to Clinical Preventive Health Care*.

RESULTS

With respect to ***cancers of the lung and bladder*** and ***superficial esophageal cancers,*** findings seem to indicate that photodynamic therapy with Photofrin® (PDT–PF) does have a therapeutic effect but that there is insufficient evidence to conclude that it has any advantage over other available treatments. With respect to the palliative treatment for ***advanced esophageal cancer,*** studies suggest, with a limited level of evidence, that the

efficacy of PDT (PF) appears to be similar to that of other palliative treatments (Nd:Yag laser ablation; metal stents). The cost of treatment with PDT (PF) is apparently much higher than that with stents. This important factor, combined with the fact that stents are easy to use and already in widespread use, diminishes both the interest in using PDT (PF) for this indication and the probability that it will be adopted in the current context. Nevertheless, PDT (PF) could be used as a complementary therapy when other treatments are contraindicated.

The recent approval of PDT (PF) in Canada for a new indication—***Barrett's esophagus***—raises important issues. A more in-depth examination will need to be conducted of the long-term efficacy of PDT for this indication and of its place in the current therapeutic arsenal, which already offers several possible treatments. These issues should preferably be reviewed in a separate assessment report.

Finally, there seems to be a near consensus in all the literature reviewed that the field of application of PDT is likely to expand and undergo many technological development, especially with respect to the photosensitizing agents used, which may lead to its increased use in the years to come. Photodynamic therapy is not expected to replace surgery, radiotherapy or chemotherapy; rather, it is meant to complement them. Still, we will need to obtain stronger scientific evidence of the advantages of PDT over other treatments and to examine its impact on the Québec health-care system before its use can be justified in these new applications.

RECOMMENDATIONS

In light of its analysis, AETMIS recommends the following:

- For the *treatment of lung and bladder cancers and superficial esophageal cancers,* PDT (PF) should be used only for clinical research purposes and should not be authorized for public coverage.

- For the *palliative treatment of advanced esophageal cancer,* PDT (PF) should be considered a possible option when recognized treatments are contraindicated and should undergo further clinical research.

- For the *treatment of Barrett's esophagus,* PDT (PF) should be fully assessed before it is introduced into current practice.

- A technology watch should be implemented to track technological advances in PDT in general and its new applications in particular.

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