Photodynamic therapy

for treating non-melanoma skin tumours

Technology Guidance from the MOH Medical Technology Advisory Committee (MTAC)

Guidance Recommendations

The Ministry of Health's MTAC has not recommended subsidising photodynamic therapy in the treatment of non-melanoma skin tumours including actinic keratosis, basal cell carcinoma, and squamous cell carcinoma in situ (or Bowen's disease).

Subsidy status

Photodynamic therapy is not recommended for subsidy in patients with the abovementioned indications.

Published on 30 September 2021

Factors considered to inform the recommendations for subsidy

Technology evaluation

1.1 The MOH MTAC ("the Committee") considered evidence presented for the technology evaluation of photodynamic therapy for non-melanoma skin tumours, including actinic keratosis (AK), basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) in situ (or Bowen's disease). The evaluation was conducted in consultation with clinical experts from the public healthcare institutions. Available clinical and economic evidence for photodynamic therapy was considered in line with the registered indication.

1.2 The evidence was used to inform the Committee's deliberations around five core decision-making criteria:

- Clinical need of patients and nature of the condition;
- Overall benefit of the technology to the patient and/or the system;
- Cost-effectiveness (value for money), which covers the incremental benefit and cost of the technology compared to existing alternatives;
- Estimated annual technology cost and the number of patients likely to benefit from the technology;
- Organisational feasibility, which covers the potential impact of adopting technology, especially barriers for diffusion.

1.3 Additional considerations, such as ethical or social issues related to adoption of the technology, may also be part of the Committee's deliberations.

Clinical need

2.1 The Committee noted that the aim of treating AK, BCC and Bowen's disease (BD) is to prevent associated morbidities such as pain or bleeding. Currently, several comparators are available in Singapore: cryotherapy and imiquimod for all three conditions; topical 5-fluorouracil (5-FU) and ingenol mebutate for AK; and surgery for BCC or BD. Surgery is invasive which is often considered when cosmetic outcome is not a concern.

2.2 The Committee noted that photodynamic therapy (PDT) is indicated for adults aged 18 years and above with the following conditions where other therapies are less appropriate:

- Thin or non-hyperkeratotic and non-pigmented actinic keratosis (AK) on the face and scalp;
- Superficial or nodular basal cell carcinoma (BCC); or

- Squamous cell carcinoma (SCC) in situ, also called Bowen's disease (BD).

AK is a precancerous form of SCC and can occur in large numbers, putting patients at risk of more serious invasive diseases. BCC and BD are the early forms of skin carcinoma and may develop into invasive or metastatic diseases.

2.3 The Committee noted that two types of PDT are available in Singapore: conventional PDT (cPDT) and daylight PDT (dPDT) using red light and daylight, respectively. Both types of PDT involve the use of a photosensitiser activated by light and induce death of premalignant or malignant cells. The photosensitiser registered with Health Science Authority (HSA) is methyl aminolevulinate (Metvix).

2.4 The Committee noted that PDT is a non-invasive procedure which can be used in outpatient setting and is easily repeatable. PDT is an alternative treatment to the currently available options for patients with large or multiple areas of affected skin. It can also be used in patients who are contraindicated for surgery, are immune-depressed or have large or multiple lesions localised in areas with poor healing ability (e.g. lower legs).

Clinical effectiveness and safety

3.1 In patients with AK, the Committee noted that, cPDT caused more pain and was likely to be associated with more adverse events (AEs) such as erythema compared with cryotherapy, imiquimod and 5-FU. Compared with imiquimod and 5-FU, cPDT showed lower treatment success rate and health related quality of life, despite better cosmetic outcomes defined by the extent of erythema, scarring, pigmentation and atrophy. Mixed results in the proportion of lesions cleared were reported, some favouring cPDT and other comparators. Compared with ingenol mebutate, dPDT showed better cosmetic outcomes but similar other effectiveness outcomes. Furthermore, compared with cPDT, dPDT was safer, less painful, and with similar effectiveness and cosmetic outcome.

3.2 In patients with BCC, the Committee noted that cPDT was less safe and less effective than surgical excision for any subtypes of BCC. Compared with surgical excision, cPDT was associated with more AEs, lower clearance rate and higher recurrence rate, despite better cosmetic outcomes. cPDT also failed to show clear superiority in safety and effectiveness over cryotherapy, 5-FU, or imiquimod. In older patients with superficial BCC located on lower extremities, cPDT might be more effective than imiquimod.

3.3 In patients with BD, the Committee noted that overall evidence was insufficient to definitively conclude on the comparative safety and effectiveness of PDT, although one trial on cPDT showed similar safety and effectiveness to clinician's choice of 5-FU or cryotherapy.

Cost-effectiveness

4.1 The Committee noted that, based on multiple published economic evidence, the cost-effectiveness of PDT in the target populations was highly uncertain in all indications studied. The inconsistency was observed in the direction and the extent of incremental benefits and costs which were shown across all comparators and populations where multiple comparative analyses were identified. Therefore, no firm conclusion can be reached on the cost-effectiveness of PDT relative to the available comparators.

4.2 The Committee noted that the economic evidence was generally of low quality and its applicability to the Singapore setting was highly uncertain. The observed variability in the economic analysis results may be attributed to the differences in the quality of data, assumptions, perspective, and methods used in the analyses.

4.3 The Committee further noted that although no local economic evidence was found, PDT was unlikely to be cost-effective in Singapore as it was more expensive than most comparators without showing clear superiority in outcomes.

Estimated annual technology cost

5.1 The Committee noted that the estimated annual cost of providing PDT service is likely to be less than $500K. Approximately 43 to 50 people with AK, BCC or BD across the public healthcare institutions would likely to receive government subsidy for PDT, if available.

Additional considerations

6.1 The Committee noted that PDT could have the potential to address the clinical need in some patients with field cancerization or lesions at challenging sites for surgery, such as periorbital regions or lips. However, other non-invasive options such as 5-FU and imiquimod, could be considered for such patients over PDT which failed to show clear superiority.

Recommendation

7.1 Based on the available evidence showing lack of superior benefits of PDT and uncertain cost-effectiveness compared to the alternatives, the Committee has not recommended subsidising photodynamic therapy for the treatment of non-melanoma skin tumours including AK, BCC and BD.

ACE
agency for
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About the Agency

The Agency for Care effectiveness (ACE) is the national health technology assessment agency in Singapore residing within the Ministry of Health. It conducts evaluations to inform the subsidy of treatments, and produces guidance on the appropriate use of treatments for public hospitals and institutions in Singapore. When using the guidance, the responsibility for making decisions appropriate to the circumstances of the individual patient remains with the healthcare professional. This guidance is based on the evidence available to the Committee as of 4 November 2020 and 17 March 2021.This guidance is not, and should not be regarded as a substitute for, professional/medical advice. Please seek the advice of a qualified healthcare professional on any medical condition.

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Chief HTA Officer
Agency for Care Effectiveness
Email: ACE_HTA@moh.gov.sg