



Complete Summary

GUIDELINE TITLE

Guidelines for topical photodynamic therapy: update.

BIBLIOGRAPHIC SOURCE(S)

Morton CA, McKenna KE, Rhodes LE, British Association of Dermatologists Therapy Guidelines and Audit Subcommittee. Guidelines for topical photodynamic therapy: update. Br J Dermatol 2008 Dec;159(6):1245-66. [229 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Morton CA, Brown SB, Collins S, Ibbotson S, Jenkinson H, Kurwa H, Langmack K, McKenna K, Moseley H, Pearse AD, Stringer M, Taylor DK, Wong G, Rhodes LE. Guidelines for topical photodynamic therapy: report of a workshop of the British Photodermatology Group. Br J Dermatol 2002 Apr;146(4):552-67. [119 references]

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SCOPE

DISEASE/CONDITION(S)

Dermatological conditions that may be treated with topical photodynamic therapy including:

- Actinic keratoses (AK)
- Bowen's disease
- Superficial, basal cell carcinoma (BCC)

GUIDELINE CATEGORY

Management
Prevention
Treatment

CLINICAL SPECIALTY

Dermatology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To review the evidence for the use of topical photodynamic therapy (PDT) in all reported dermatological indications and interpret how this modality might best be used in clinical practice, using the same validated scoring system as in the previous guideline

TARGET POPULATION

Adults and children undergoing photodynamic therapy for dermatological conditions

INTERVENTIONS AND PRACTICES CONSIDERED

Management/Treatment

1. Cutaneous photodynamic therapy (PDT)
 - Topical application of photosensitizing agents:
 - 5-aminolaevulinic acid (ALA)
 - Methyl aminolaevulinate (MAL)
 - Light sources and dosimetry
2. Topical PDT in nonmelanoma skin cancer
3. Topical PDT for infectious and inflammatory dermatoses

MAJOR OUTCOMES CONSIDERED

- Disease remission/resolution
- Recurrence rate
- Cosmetic outcome
- Photoaging
- Adverse effects of treatment
- Cost effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

I: Evidence obtained from at least one properly designed, randomized controlled trial

II-i: Evidence obtained from well-designed controlled trials without randomization

II-ii: Evidence obtained from well-designed cohort or case-control analytical studies, preferably from more than one centre or research group

II-iii: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments could also be regarded as this type of evidence.

III: Opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

IV: Evidence inadequate owing to problems of methodology (e.g., sample size, or length of comprehensiveness of follow-up or conflicts in evidence)

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendation Grades

- A. There is good evidence to support the use of the procedure.
- B. There is fair evidence to support the use of the procedure.
- C. There is poor evidence to support the use of the procedure.
- D. There is fair evidence to support the rejection of the use of the procedure.
- E. There is good evidence to support the rejection of the use of the procedure.

COST ANALYSIS

Photodynamic Therapy: Cost Assessment

The original guidelines provided a detailed cost-comparison of 5-aminolaevulinic acid photodynamic therapy (ALA-PDT) with standard therapy derived from two studies of Bowen's disease (BD). Estimated costs for ALA-PDT were comparable with cryotherapy and topical 5-fluorouracil (5-FU) when morbidity costs were included, but reflected the use of a nonlicensed ALA preparation and light sources no longer in routine use. A cost-minimization study of six treatments commonly used for BD in the United Kingdom (U.K.) National Health Service concluded that ALA-PDT was the most expensive option for treating a single lesion, but considered average costs for three light sources now rarely used, including laser, making extrapolation difficult to current practice of PDT. The cost of topical PDT will be influenced by clinic set-up, opportunities for safe multiple use of the same package for more than one lesion/patient, nurse/technician- vs. doctor-led therapy, use of relatively low-cost light-emitting diode (LED) sources, etc. A discrete choice survey of members of the general public in Australia demonstrated that preference for avoidance of scarring was considered to be more important even than lesion response, with a willingness to pay more for methyl aminolaevulinate photodynamic therapy (MAL-PDT) over simple excision for basal cell carcinoma (BCC).

A recent detailed economic evaluation of topical MAL-PDT, based on multicentre comparison trials for actinic keratoses (AK), superficial and nodular BCC, calculated the cost per full responder, defined as clearance of all lesions in a patient and an excellent cosmetic outcome. The authors concluded that PDT is a cost-effective intervention in AK when compared with cryotherapy over 1 year, and better value for money than excision in BCC when compared over 5 years (to allow time for recurrences). This industry-sponsored study took into account response rates, possible recurrence and cosmesis as well as estimating the costs of managing nonresponse, recurrence and nonexcellent cosmetic outcome, and represents the most detailed consideration, to date, of the relative cost of PDT when a value on cosmetic outcome benefit is included.

Novel methods of delivering topical PDT could improve its cost-effectiveness. The cost-effectiveness of delivering topical PDT in a community setting was demonstrated in a small randomized study using a portable PDT light source, with therapy delivered by a nurse, permitting a more convenient service for typically elderly patients presenting with BD and BCC. Ambulatory PDT could minimize hospital resources as well as offer treatment at /closer to home using portable LED devices. Further studies are required to update cost-effectiveness analysis for topical PDT as currently used in the U.K. National Health Service, with particular consideration to its use in multiple and/or large lesions/field treatments.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

These guidelines represent an update, commissioned by the British Association of Dermatologists Therapy Guidelines and Audit Subcommittee, of those originally produced from a workshop held in November 2000 by the British Photodermatology Group.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence (**I-IV**) and strength of recommendation ratings (**A-E**) are defined at the end of the "Major Recommendations" field.

Photosensitizing Agents

Topical application of the prodrugs 5-aminolaevulinic acid (ALA) and methyl aminolaevulinate (MAL) is effective in cutaneous photodynamic therapy (PDT) (*Strength of Recommendation A, Quality of Evidence I*).

Light Sources and Dosimetry

Currently, a range of light sources, doses and irradiances continues to be used in ALA-PDT, whereas in MAL-PDT the standard procedure now typically involves a light-emitting diode (LED) source. A range of continuous wave light sources is effective in topical PDT (*Strength of recommendation A, Quality of evidence II-iii*).

Topical Photodynamic Therapy in Nonmelanoma Skin Cancer

Actinic Keratoses

Topical PDT is an effective therapy for thin and moderate thickness actinic keratoses (AK), with superiority to cryotherapy depending on protocol. Efficacy is relatively poorer for acral lesions, but PDT may still offer therapeutic benefit. Cosmetic outcome following PDT for AK is superior to cryotherapy (*Strength of recommendation A, Quality of evidence I*).

Bowen's Disease (BD)

Topical PDT is an effective therapy for BD, with equivalence to cryotherapy and equivalence or superiority to topical 5-fluorouracil (5-FU). Cosmetic outcome is superior to standard therapy. Topical PDT offers particular advantages for large/multiple patch disease and for lesions at poor healing sites (*Strength of recommendation A, Quality of evidence I*).

Squamous Cell Carcinoma (SCC)

The high efficacy of topical PDT for in situ SCC, and the efficacy figures reported particularly for superficial invasive lesions limited to papillary dermis, suggest that depth of therapeutic effect is the limiting factor for PDT in invasive SCC, with further study required. Current evidence supports the potential of topical PDT for superficial, microinvasive SCC, but in view of its metastatic potential, topical PDT cannot currently be recommended for the treatment of invasive SCC (*Strength of recommendation D, Quality of evidence II-iii*).

Basal Cell Carcinoma (BCC)

Topical MAL-PDT and ALA-PDT are effective treatments for superficial BCC (*Strength of recommendation A, Quality of evidence I*). Topical MAL-PDT is effective in nodular BCC, although with a lower efficacy than excision surgery, and may be considered in situations where surgery may be suboptimal (*Strength of recommendation B, Quality of evidence I*).

Cutaneous T-cell Lymphoma (CTCL)

Topical PDT can elicit a response and has a potential role in the treatment of localized CTCL. Further studies of PDT for CTCL are required to define optimal treatment parameters (*Strength of recommendation C, Quality of evidence II-iii*).

Intraepithelial Neoplasia of the Vulva and Anus

Topical PDT offers therapeutic benefit in vulval intraepithelial neoplasia (VIN), but refinement of practical aspects of delivery and optimization of protocol are required (*Strength of recommendation C, Quality of evidence II-iii*).

Extramammary Paget's Disease (EMPD)

Topical PDT, although potentially effective in EMPD, is currently associated with high recurrence rates in the limited cases reported (*Strength of recommendation C, Quality of evidence III*).

Photodynamic Therapy for Skin Cancer Prophylaxis

Hence, current evidence indicates that topical PDT has the potential to provide a preventive role although further evidence is required to clarify its mechanism of action (*Strength of recommendation C, Quality of evidence IV*).

Photodynamic Therapy in Organ Transplant Recipients (OTRs)

Current evidence suggests that topical PDT, although showing lower efficacy than in immunocompetent individuals, may provide a useful therapy for epidermal dysplasias in OTRs (*Strength of recommendation B, Quality of evidence I*).

Topical Photodynamic Therapy for Infectious and Inflammatory Dermatoses

Acne and Related Conditions

Although topical PDT can improve inflammatory acne on the face and back, optimization of protocols, to sustain response while minimizing adverse effects, is awaited (*Strength of recommendation B, Quality of evidence I*).

Viral Warts

Recent studies continue to support the potential of topical PDT in viral warts, particularly plantar warts, but it appears a relatively painful therapy option, with outcomes dependent on adequate paring and the use of a keratolytic agent pre-PDT (*Strength of recommendation B, Quality of evidence I*).

Genital Warts

Topical PDT may be considered as a treatment option for patients with genital warts (*Strength of recommendation B, Quality of evidence I*).

Cutaneous Leishmaniasis

Current evidence suggests that topical PDT is effective in clearing lesions of cutaneous leishmaniasis although further studies with culture confirmation of amastigote clearance are required (*Strength of recommendation B, Quality of evidence I*).

Psoriasis

Overall, current evidence, combined with studies reviewed in our previous guidelines, does not support the use of topical ALA-PDT as a practical therapy for psoriasis (*Strength of recommendation D, Quality of evidence I*).

Photodynamic Photorejuvenation

Interest is clearly gathering in this area, although at present there is a need for well-designed randomized, controlled, adequately powered studies with a longer follow up and ideally histological confirmation of clinical findings. The relative roles of PDT and intense pulsed light (IPL) as treatment/adjunctive treatment are anticipated to undergo further exploration. Standard topical PDT (continuous wave light source) and ALA-IPL appear effective in photorejuvenation (*Strength of recommendation B, Quality of evidence II-iii*).

Table: Clinical Indications for Topical Photodynamic Therapy in Dermatology: Recommendations and Evidence Assessment

Strength of Recommendation	Quality of Evidence	Indication
A	I	<ul style="list-style-type: none"> • Thin and moderate thickness actinic keratoses • Bowen's disease • Superficial basal cell carcinoma
B	I	<ul style="list-style-type: none"> • Thin nodular basal cell carcinoma • Epidermal dysplasias in organ transplant recipients • Inflammatory acne on the face and back • Viral warts, particularly plantar warts • Genital warts • Cutaneous leishmaniasis
B	II-iii	Photorejuvenation
C	II-iii	<ul style="list-style-type: none"> • Localized cutaneous T-cell lymphoma • Vaginal intraepithelial neoplasia
C	III	Extramammary Paget's disease
C	IV	Skin cancer prevention
D	I	Psoriasis
D	II-iii	Invasive squamous cell carcinoma

Adverse Effects

Acute

Pain is a common feature during light exposure in PDT, but topical PDT is overall a well-tolerated treatment modality with a low rate of serious acute adverse events (*Strength of recommendation A, Quality of evidence I*).

Application of topical anaesthetics is of limited use for pain relief during light exposure of AK (*Strength of recommendation D, Quality of evidence II-i*).

Carcinogenicity

Topical PDT has a low risk of carcinogenicity and reported cases of skin cancer occurring in relation to this therapy are rare (*Strength of recommendation A, Quality of evidence II-iii*).

Definitions:

Levels of Evidence

I: Evidence obtained from at least one properly designed, randomized controlled trial

IIi: Evidence obtained from well-designed controlled trials without randomization

IIii: Evidence obtained from well-designed cohort or case-control analytical studies, preferably from more than one centre or research group

IIiii: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments could also be regarded as this type of evidence.

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Recommendation Grades

- A. There is good evidence to support the use of the procedure.
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- D. There is fair evidence to support the rejection of the use of the procedure.
- E. There is good evidence to support the rejection of the use of the procedure.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate treatment with topical photodynamic therapy in clinical practice

POTENTIAL HARMS

Acute

- The most common and troublesome acute adverse event of topical photodynamic therapy (PDT) is the burning or stinging pain that occurs during light exposure, and may continue postexposure in a minority. Pain is restricted to the illuminated area and may reflect nerve stimulation and/or tissue damage by reactive oxygen species (ROS), possibly aggravated by hyperthermia. Treatment of psoriasis and viral warts in particular is frequently limited by pain. Pain appears more intense in large area lesions, with actinic keratoses, Bowen's Disease and basal cell carcinoma (BCC) covering an area of > 130 mm² significantly more painful to treat.
- Caution has been advised in treating large skin fields by PDT in case of pronounced phototoxic reaction, with the option to consider initial small-area PDT prior to large-field exposure. Application of topical anaesthetics is of limited use for pain relief during light exposure.

Chronic

The incidence of scarring associated with topical PDT is very low. Postinflammatory hypopigmentation or hyperpigmentation can occur following PDT. Hair loss is a potential side-effect of PDT as concomitant sensitization of the pilosebaceous unit takes place.

Carcinogenicity

Topical PDT has a low risk of carcinogenicity and reported cases of skin cancer occurring in relation to this therapy are rare.

Safety Aspects of Topical Photodynamic Therapy

- Blue light can pose a hazard to the retina, potentially causing irreversible damage to the photosensitive neurotransmitters in the macula. However, most PDT is carried out using red light which is not phototoxic to the retina. Nevertheless, the wearing of goggles for both patient and staff is recommended to limit the transmission of high-intensity light and to avoid discomfort and disturbance of colour perception.
- Following topical PDT, localized photosensitivity can remain for up to 48 hours, a formulation of 5-aminolaevulinic acid (ALA) degrading with a half-life of about 24 hours and methyl aminolaevulinate (MAL)-induced protoporphyrin IX (PpIX) clearing from normal skin within 24–48 hours.

CONTRAINDICATIONS

CONTRAINDICATIONS

Contraindications to photodynamic therapy include a history of porphyria and allergy/photoallergy to active ingredients of the applied photosensitizer.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These guidelines have been prepared for dermatologists on behalf of the British Photodermatology Group and the British Association of Dermatologists and are based on the best data available at the time the report was prepared. Caution should be exercised when interpreting the data where there is a limited evidence base; the results of future studies may require alteration of the conclusions or recommendations in this report. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. Just as adherence to guidelines may not constitute defence against a claim of negligence, so deviation from them should not necessarily be deemed negligent.
- This article represents a planned regular updating of the original guidelines for the use of topical photodynamic therapy. Detailed discussion of studies evaluated in the previous paper will not be repeated except where comparison with new evidence is necessary. This may entail a disproportionate weight being given to more recent techniques and studies, but strength of evidence recommendations (see Appendix 1 in the original guideline document) take into account all available information.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Morton CA, McKenna KE, Rhodes LE, British Association of Dermatologists Therapy Guidelines and Audit Subcommittee. Guidelines for topical photodynamic therapy: update. Br J Dermatol 2008 Dec;159(6):1245-66. [229 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Apr (revised 2008 Dec)

GUIDELINE DEVELOPER(S)

British Association of Dermatologists - Medical Specialty Society

SOURCE(S) OF FUNDING

British Association of Dermatologists

GUIDELINE COMMITTEE

British Association of Dermatologists Therapy Guidelines and Audit Subcommittee

British Photodermatology Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

CAM has received honoraria for speaking, organized educational events and conducted research for Galderma, PhotoCure and Phototherapeutics Ltd.

GUIDELINE STATUS

This is the current release of the guideline.

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photodynamic therapy: report of a workshop of the British Photodermatology Group. Br J Dermatol 2002 Apr;146(4):552-67. [119 references]

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [British Association of Dermatologists Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

Possible audit points are included in the [original guideline document](#).

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on April 22, 2005. The information was verified by the guideline developer on August 2, 2005. This NGC summary was completed by ECRI Institute on June 4, 2009. The updated information was verified by the guideline developer on June 18, 2009.

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