

Table 19.2: Indications for UVB and PUVA

Condition	Comment
Established major indications	
Psoriasis	Consider PUVA if UVB disappointing (for example, short remission)
Atopic dermatitis	PUVA very rarely justified in childhood (but consider before systemic immunosuppression)
Polymorphic light eruption	PUVA is more effective than broadband UVB, so consider if narrowband UVB unavailable
Vitiligo	UVB (narrowband) probably as effective as PUVA
Mycosis fungoides	UVB for patch stage; PUVA for plaque stage
Other indications (less frequently treated, less evidence of effectiveness)	
Dermatitis other than atopic dermatitis	Very limited study evidence: UVB to be preferred, except for palm and sole dermatoses for which PUVA may be better
Chronic urticarias	Limited study evidence
Acne vulgaris	Broadband UVB at erythemogenic doses (mainly of historic interest now that more effective therapies are available)
Pityriasis rosea	UVB effective but rarely required
Pityriasis lichenoides chronica	UVB treatment of choice
Generalized itch	Good evidence for efficacy of UVB particularly in itch of kidney failure, but can be useful even for “idiopathic pruritus”
Lichen planus	No comparative studies, but narrowband UVB often effective for widespread disease; PUVA for severe palmar involvement
Granuloma annulare	Both UVB and PUVA may clear this
Necrobiosis lipoidica	PUVA possibly effective (ulcer healing, and perhaps changing texture towards normal, as well as camouflaging)
Pityriasis rubra pilaris	PUVA sometimes useful; almost invariably exacerbated by UVB

Indications for UVB or PUVA

Psoriasis

Psoriasis (214, 215) is the most common indication for UVB and for PUVA. PUVA is more effective than broadband UVB, but not much different in efficacy compared to narrowband UVB. In general, PUVA is used only when UVB, administered appropriately, fails to adequately clear psoriasis or when the duration of remission is short. In view of the cumulative exposure-related skin cancer risks known to be associated with PUVA, UVB is preferred, particularly for younger patients. Neither therapy is curative, and remissions of on average 6 months can be expected (Table 19.3).

When is UVB indicated?

- For patients who have extensive disease on limbs and body which makes practical use of topical therapy difficult.
- If topical therapy has not worked.

When should PUVA be used instead of UVB?

- If UVB is ineffective.
- If the duration of remission following three consecutive UVB courses is consistently short (for example, <2 months).
- For palmoplantar pustular psoriasis, PUVA appears more effective.

Atopic dermatitis

UVB and PUVA are effective treatments for atopic eczema/dermatitis. The rules for psoriasis can broadly be applied to this condition. It is used:

- for particularly extensive truncal and limb eczema
- when standard topical therapies are not controlling activity or only resulting in short-term remissions
- as steroid-sparing therapy when potent or very potent topical steroids are otherwise required continuously to maintain disease control.

As for psoriasis PUVA should be reserved for older patients and those who are not helped by UVB. In general, treatment courses often have to be more gentle, with lower increments and more prolonged in comparison to those used for psoriasis (Table 19.4).

Topical therapy with corticosteroids should be continued, although the need for this will reduce as the disease is brought under control with phototherapy. If your phototherapy



214, 215: Psoriasis before (214) and after (215) a course of narrowband UVB.



department is not air-conditioned, then heat particularly in the summer months may be a reason for apparent treatment failure, because sweating can be a factor in aggravating the eczema.

Polymorphic light eruption

Mild polymorphic light eruption (PLE) (see Chapter 5) is usually managed with advice on behavioral, clothing, and topical sunscreen photoprotection measures. However, when it is more severe and impairing life quality, prophylactic PUVA or UVB phototherapy administered in spring is beneficial. Narrowband UVB is as effective as PUVA, and generally preferable for its convenience and greater safety. However, PUVA is more effective than broadband UVB. Patients need to know before starting treatment that it is common for PLE to be provoked during the course. This can usually be managed by adjusting the doses used, treating only sites requiring therapy (for example, treating patients wearing shorts and a T-shirt, the same ones each treatment), and if necessary applying a potent topical corticosteroid immediately after each treatment. If PLE is very readily provoked by UVB, then PUVA may be better, and vice versa. Reasons for failure are given in Table 19.5.

Table 19.3: Phototherapy for psoriasis

- Narrowband UVB is more effective than broadband UVB for psoriasis.
- Narrowband UVB and PUVA are of similar efficacy for psoriasis.
- For convenience and safety reasons narrowband UVB is the first choice phototherapy for psoriasis.

Table 19.4: Phototherapy for atopic dermatitis

- Phototherapy for atopic dermatitis requires a “gentler” regimen than for psoriasis.
- It is important that flares of atopic dermatitis are treated as usual during a phototherapy course.
- Although one indication for phototherapy for atopic dermatitis is to reduce topical steroid requirements, it is important that these are not withdrawn too early.
- Improvement of atopic dermatitis with phototherapy is often not apparent until 15–20 treatments have been given.

Table 19.5: Common reasons for “failure” of prophylactic phototherapy for PLE

- Given at suboptimal time of year (too early or too late).
- Attempts to treat normally covered sites that do not require treatment.
- Failure to manage induced PLE during a treatment course (with dose adjustments, topical corticosteroids immediately after treatments if necessary).

Cutaneous T cell lymphoma (mycosis fungoides)

The effect of PUVA on the long-term prognosis of cutaneous T cell lymphoma (CTCL) is unknown. The finding of “solar signature” *p53* mutations in tumor stage CTCL raises possible concerns about use of phototherapy and photochemotherapy, although there is no evidence to suggest that treatment with either adversely affects the natural history. If simple treatment approaches with topical steroids have been unhelpful, PUVA is an effective treatment for symptomatic (pruritic) early stage I and Ia patch and plaque disease (Table 19.6). The effect appears to be localized to exposed sites, and “sanctuary site” disease does not clear (216, 217). It is also useful, sometimes in combination with other therapies such as retinoids or interferon, in the palliation of later stage disease. Narrowband UVB is effective for patch stage disease but once lesions are palpably thickened PUVA is more likely to be effective.

Table 19.6: Phototherapy for mycosis fungoides

- No treatments for mycosis fungoides are known to alter prognosis.
- The simplest safest treatment that controls symptoms should be chosen.

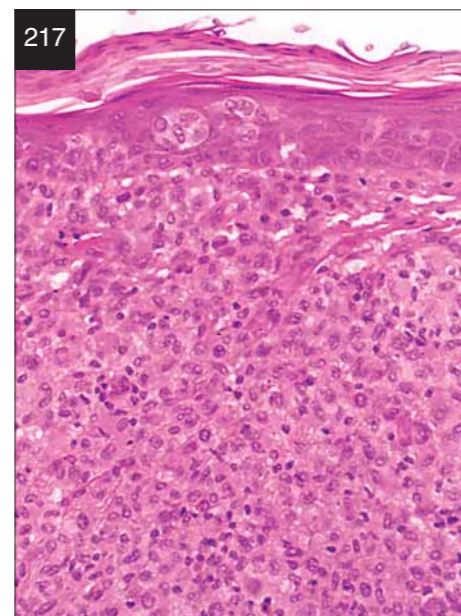


216: Sanctuary site mycosis fungoides developing in sites covered by genital protection worn during PUVA by this patient whose mycosis fungoides elsewhere cleared well.

217: Histopathology of biopsy taken from sanctuary site skin shown in 19.3.
218: Vitiligo responding to narrowband UVB phototherapy. Note the follicular pigmentation and the accentuation of brown pigment around the lesion's periphery – patients must be warned this often occurs with PUVA (probably less often with NB-UVB) and can make affected skin areas more noticeable.

Vitiligo

Narrowband UVB and PUVA can both induce repigmentation. Up to 70% of patients with vitiligo benefit if they are treated continuously for a year or more. Those with trichrome pattern vitiligo, that is those with areas of reduced pigment as well as areas of normal skin and of complete pigment loss, tend to respond better. Acral sites respond poorly. Patients repigment in a perifollicular fashion initially (218). In patients with skin phototypes II–V, there is a danger that, if complete repigmentation does not occur, the problem will be made worse by exaggeration of contrast between vitiligo and surrounding skin, and there could be scattered macules of follicular pigment if partial repigmentation occurs. However, if the patient is well motivated, has a good understanding of their condition and what to expect from this treatment, and has a pattern of vitiligo that is likely to respond, then UVB or PUVA can greatly



improve quality of life. Some of those in whom successful repigmentation is achieved keep their pigmentation after an initial prolonged course of treatment, but others lose it again and require repeated courses (Table 19.7).

It should be remembered that a course of PUVA for vitiligo may easily give a patient a high cumulative dose with 150–200 treatments given twice weekly over 1–2 years. A frank discussion with the patient of the risks of therapy – the risk of more pronounced lesional adverse effects with “burning” and blistering, and the possibility of an increased skin cancer risk compared to unaffected skin – is a must before embarking on prolonged courses of phototherapy for vitiligo.

Contraindications to UVB or PUVA

There are a few absolute contraindications, particularly in those who:

- are medically unfit – for example, those with severe cardiovascular or respiratory disease that prevents standing in the treatment cubicle, or that could be destabilized should an unexpected sunburn-like erythema occur
- have lupus erythematosus
- have genophotodermatoses, for example xeroderma pigmentosum (see Chapter 17)
- are pregnant (a contraindication to systemic PUVA, but not to UVB).

Relative contraindications include:

- a personal history of skin cancer
- those with atypical nevus syndrome
- a family history of skin cancer (melanoma or non-melanoma skin cancers at an unusually young age)
- previous exposure to radiotherapy
- medications that may interact with psoralens (for PUVA), or that may be photo-active in UVB range (for UVB) (these are usually not a problem as long as pretreatment minimal phototoxic dose (for PUVA) or minimal erythematol dose (for UVB) testing is performed)
- young age, because of long-term risks – PUVA should usually be avoided in children
- those with photo-induced epilepsy or poorly controlled epilepsy – well-controlled epilepsy, not known to be triggered by fluorescent lamp exposure, is not a contraindication, but the nurse phototherapist needs to be in line of eye and verbal contact with the cubicle during treatment to ensure patient safety.

Table 19.7: Phototherapy for vitiligo

- Narrowband UVB and PUVA can both be effective for vitiligo.
- Prolonged courses are required.
- Therefore, patients must be well motivated, knowledgeable about the likelihood of success or failure, and fully aware of potential adverse effects.

How are phototherapy and photochemotherapy administered?**Before starting treatment with UVB or PUVA****Patient assessment**

The patient is referred from the dermatology outpatient clinic to the phototherapy unit with a completed referral and consent form. A risk factor profile including previous phototherapy or PUVA treatments, sun exposure history, occupation, personal and family history of skin cancer, and medication taken during the previous 6 months is included in the information on this form. Examination establishes disease extent, and any evidence of photodamage, nevi, any skin cancers or precancerous lesions (such as solar keratoses), and vitiligo is recorded.

Patient education

An information sheet explains the treatment protocol, advises use of appropriate emollients (that is, emollients without sun barrier properties, and also without fragrances or other possibly photo-active ingredients), and explains both acute and chronic adverse effects of treatment. The treatment cabinet is demonstrated, and advice given on the need for consistency of hairstyle and dress during the course of phototherapy to avoid unexpected erythema reactions. Patients are asked to sign a consent form before beginning treatment.

Dosimetry

For hospital-based practice, if there is a local medical physics department, then it is important that UVB and UVA cubicle outputs are regularly checked with an appropriately calibrated meter, used according to standardized methods, and that checks are made whenever the cubicle output might have changed significantly – for example, if more than one or two lamps need to be changed. Only if outputs are measured accurately is it possible to be sure that doses are being administered as prescribed. It has been our experience that in-built cabinet dosimeters can be unreliable, although for office-based practice they may have to be relied upon if there is not ready access to external calibration checks.

According to local protocols we regularly check the irradiance of all phototherapy equipment, and whenever tubes are changed, and with the use of the simple formula below we amend a table of doses and corresponding exposure times accordingly (see Chapter 3).

$$\text{irradiance (mW/cm}^2\text{)} \times \text{time (seconds)} = \text{dose (mJ/cm}^2\text{)}$$

Documentation

The dose given, adverse effects, and response to treatment are recorded at each visit. The cumulative dose, numbers of exposures, adverse effects, and efficacy of treatment are typed into the database and a summary sheet is placed at the front of the phototherapy notes. When the patient finishes a course of phototherapy (or PUVA) a copy of this summary sheet is put in the patient’s main hospital notes.

UVB phototherapy regimen

Treatment regimen

The optimum treatment regimen for each UVB-responsive condition has yet to be defined. However, recent and ongoing research should ensure that, in the future, the use of UVB phototherapy is based even more firmly on evidence, rather than anecdote and tradition.

It is useful to consider the various variables that alter treatment efficacy and safety, in conjunction with the ideals we are aiming for when prescribing UVB.

Variables in UVB phototherapy

These include:

- ultraviolet source - the properties of the lamps used, especially the spectrum of wavelengths emitted
- starting dose
- treatment frequency
- dose increments.

Our aim is to adjust the above variables to achieve:

- effective clearance of the condition, with prolonged remission
- minimization of side effects (both acute and chronic)
- low cumulative number of exposures to clearance (and over each patient’s lifetime)
- low cumulative dose
- short exposure times
- low cost.

Other factors influencing the treatment regimen include:

- condition treated, and
- patient characteristics, for example skin phototype.

Over the past decade, most progress has been made in the treatment of psoriasis, the condition for which we have most evidence about how to use UVB phototherapy. We know that:

- the narrowband UVB lamp is more effective than broadband UVB. While narrowband UVB in common with all UVB sources will predictably produce erythema, it appears to be the case that suberythemogenic doses will clear psoriasis (see the next two points). On the basis of evidence from animal studies and knowledge of how the treatment is currently used, it is likely (but not certain) to prove safer regarding long-term non-melanoma skin cancer risk
- on safety grounds, and for patient convenience (avoiding unnecessary visits to the department), we base our starting dose on a percentage of each individual’s minimal erythema dose (MED)
- a recent study comparing a low and a high incremental dosage regimen favored the low incremental dosage regimen (which is shown below)
- for the majority of patients (of Fitzpatrick skin phototypes I–III of a Northern European population) a three-times weekly treatment is to be preferred to a five-times weekly treatment.

A current standard treatment regimen is shown in *Table 19.8*. Expected average (median) number of exposures for effective treatment is shown in *Table 19.9*.

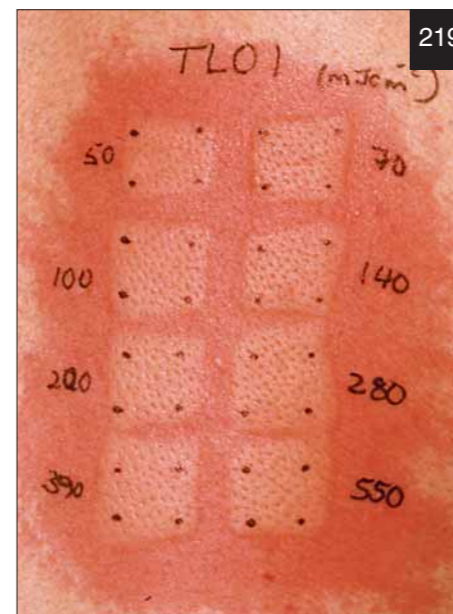
Table 19.8: Standard UVB phototherapy regimen

Dose	Amount
Initial	50% or 70% of MED*
Subsequent doses (thrice weekly)	psoriasis (in increments of 20%** of previous dose) atopic eczema (in increments of 20%** of previous dose) desensitization (in increments of 20%** of previous dose)

*The optimal percentage of MED starting dose has not been determined).
** Reducing to 10%, depending on erythema response: it is important to ask about reactions to previous treatment, and make a skin examination. This can be done usually by an experienced phototherapy nurse in a well-lit room, at each visit.

Minimal erythema dose (MED) determination

Ideally, an attempt should be made to individualize the starting dose by basing it on MED assessment. In the UK, the MED is defined as the dose of radiation that produces minimal erythema at 24 hours post irradiation. Elsewhere, a different definition (the dose that causes well-defined erythema) is used. There is a poor correlation between the MED and skin type. Determining the MED allows a safe, but not too low, UV starting dose to be administered to each patient. Although the most frequent acute adverse effect that can be avoided by basing starting dose on the MED is erythema, occasionally



219: Solar urticaria unexpectedly revealed in a night-worker about to start narrowband UVB for atopic dermatitis.

the MED testing reveals unexpected severe photosensitivity, such as solar urticaria (219) or chronic actinic dermatitis. Such testing may also show the papular response typical of polymorphic light eruption. (220).

It may be impractical in some units to perform MEDs and an empiric starting dose may be used. This should be carefully chosen based on knowledge of the local skin type population and should always be well below the likely erythema threshold for the majority of patients.



220: This patient was about to start prophylactic treatment for polymorphic light eruption, but this papular response (most marked at 140 mJ/cm²) is also seen from time to time on MED-testing patients about to start treatment for other conditions, such as psoriasis. A response like this does not preclude effective and safe NB-UVB phototherapy but indicates that caution may be required with dose increments (particularly in the psoriasis patient who is a positive Köbner reactor).

Table 19.9: Expected average (median) number of exposures for effective treatment

Condition	Median number of exposures
Psoriasis	20–25
Atopic eczema	30–35
Polymorphic light eruption	15
Chronic urticaria	35
Generalized pruritus	25

Method

If a separate irradiation source (221) is used to determine the MED, it must contain the same type of lamps as those in the UVB cabinet, and dosimetry must be accurate. In some centers the treatment cabinet itself is used (222), although this has disadvantages:

- treatments cannot be given while MED assessment irradiations are performed
- it is time-consuming to cover patients up adequately to safely perform MED irradiations in the cubicle
- some patients (for example, young children and claustrophobic people) may be unable to cope with MED irradiations in the cubicle.

MED is usually determined on back, forearm or buttock skin (preferred site varies between units). In Dundee, a template of eight 1 x 1 cm squares is affixed to the back of the patient

and each square is exposed to a different dose of radiation. The remainder of the patient must be covered during these exposures. The selection of exposure doses is based on the skin type of the individual. For example, for narrowband UVB, doses of 25, 50, 70, 100, 140, 200, 280, 390 mJ/cm² (Dundee doses, external meter calibration) are used for skin phototype I and II patients, but the first two doses are omitted and doses of 550 and 770 mJ/cm² added for higher phototype patients. The erythema response to these exposures is evaluated at 24 hours. Note the geometric series of doses chosen: there are theoretic reasons, based on the UVB-erythema dose-response curve, to use such a series and not a straight arithmetic series. In practice, the main problem with a simple arithmetic series is that with most such series (for example, 70, 80, 90, 100, 110, 120 mJ/cm²) the maximum dose will be below the MED for a significant minority of patients, who will be under-treated as a result.

Why assess MED?

The starting dose is not routinely based on MED determination, which does require accurate dosimetry and well-trained staff, in all centers. However, when practicable, the starting dose should be MED based as assessing the MED allows us to:

- give an individualized, appropriate dose to each patient
- maximize therapy and therefore reduce number of exposures required to clear
- allow for photo-active medication
- allow for tanning or extensive vitiligo (MED being assessed on a patch of vitiligo)
- identify unsuspected photodermatoses, for example lupus erythematosus, chronic actinic dermatitis syndrome or solar urticaria.

Potential pitfalls in assessing the MED

We use the following points to guide treatment.

- Oral or topical steroid therapy will suppress the erythema response to radiation.
- The mid-back is generally the favored site because the forearm registers a higher MED.
- If a patient is tanned, one must take into account any non-pigmented sites (for example, buttocks or patches of vitiligo). The starting dose of UVB for vitiligo should whenever possible be based on determining the MED on a depigmented patch.

PUVA photochemotherapy regimen**Choice of psoralen and its route of administration**

The psoralen most widely used is 8-methoxypsoralen (8-MOP), administered by mouth. If the microcrystalline tablet formulation is used, UVA treatment is usually given 2 hours after the tablets (0.6 mg/kg or a dose based on a surface area nomogram) are taken. Nausea is a frequent side effect of 8-MOP: this is usually not a problem if the tablets are taken with food, but some patients need to be changed to 5-methoxypsoralen (5-MOP) tablets which rarely, if ever, cause this adverse effect. It is because it is not certain that 5-MOP PUVA is as effective as 8-MOP PUVA (and 5-MOP is more expensive) that 8-MOP is generally the standard first-line psoralen.

The psoralen can also be administered topically, by application as a bath-water solution for whole-body treatment or as soaks, paint or cream for localized treatment (for example, for hands and feet). In the UK, 8-MOP is the psoralen currently most

widely used for bath PUVA, although in some areas trimethylpsoralen (TMP) is favored. Bath PUVA is more time-consuming for patients and staff than oral PUVA, but may be preferred when the patient is on medications, such as warfarin, which might interact with an oral psoralen or if the eye protection necessary for oral PUVA will be particularly problematic. Also, when psoralens are applied topically they reach a higher skin concentration, and shorter UVA exposures are needed for the same effect: this is particularly true for TMP, and is an advantage if short treatment times are important (for example, for very frail or claustrophobic patients), but can be a disadvantage in that the risk of phototoxic erythema reactions after natural sunlight UVA exposure is greater.

Starting dose – minimal phototoxic dose (MPD) determination

The starting dose should ideally be based on each individual's minimal phototoxic dose. The reasons for doing this are similar to those described for performing MED testing before UVB phototherapy. Additionally, for oral PUVA, MPD assessment ensures that the psoralen dose given does cause a phototoxic reaction. If it does not then MPD testing should be repeated after an increased psoralen dose or a switch to topical PUVA made. Although not ideal, oral PUVA is sometimes started at a low UVA dose without prior MPD determination. Bath PUVA should never be started without the MPD being determined first because of the particularly severe photosensitivity that can result, and which cannot be predicted by skin phototype or any other patient characteristics.

Frequency of treatment

Treatment with PUVA is normally twice weekly (based on the time course of PUVA erythema, which peaks later than UVB erythema), although in some countries thrice-weekly treatment is customary. When necessary for patient convenience, once-weekly treatment can also be effective, although it takes longer to see benefit.

Special precautions

Patients treated with PUVA need to be careful to avoid natural UV exposure (including exposure through window-glass and cloud) throughout the course. Following psoralen tablets, eye protection (UVA-absorbing spectacles) is advised for 24 hours, and following bath psoralen application if an inflammatory dermatosis treated is very extensive (and significant systemic absorption possible), to minimize the risk that a psoralen-UVA reaction in eye lenses could lead to cataracts.



221: Using a bank of narrow-band UVB lamps separate from the cubicles used for treatment makes MED testing more convenient for patients and staff and, in a sufficiently staffed unit, allows MED testing to be conducted while phototherapy for other patients is ongoing. It does require careful dosimetry to ensure that doses administered using the separate bank of lamps correspond to those that will be administered in the treatment cubicle.



222: MED testing using the door of a treatment cubicle where a separate bank of the appropriate tubes was not available.