European Dermatology Forum

# Guideline on Vitiligo

Developed by the Guideline Subcommittee “Vitiligo” of the
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**EDF-Guidelines for Vitiligo**

# By the writing group of the Vitiligo European Task Force (VETF) in cooperation with the European Academy of Dermatology and Venereology (EADV) and the Union Européenne des Médecins Spécialistes (UEMS)

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*What is already known about this topic?* Vitiligo is a disease lacking definitive and completely effective therapies. Phototherapy and combined treatments are the most effective treatments.

*What is the goal of the treatment in vitiligo?* Therapy should stop the progression of the lesions and provide complete or almost complete repigmentation to be satisfactory for the patient. The results should be maintained over time.

*What does this study add?* The criteria for treatment have been critically reviewed. Evidence-based recommendations (S1) for the treatment of vitiligo have been made. A proposal for clinical evaluation, treatment and follow-up has been outlined.

**Abbreviations and Explanations**

RCT, Randomized Controlled Trial

VETF, Vitiligo European Task Force

SV, Segmental Vitiligo

NSV, Nonsegmental Vitiligo

TCS, Topical Corticosteroid

TIM, Topical Immunomodulating Macrolactams

TCI, Topical Calcineurin Inhibitor

PUVA, Psoralens plus UVA

UVA, Ultraviolet A

UVB, Ultraviolet B

NB UVB, Narrow Band UVB (311 nm)

KUVA, Khellin plus UVA

MED, Minimal Erythemal Dose

OMP, Oral Minipulses

MBEH, Monobenzone ethyl ester (or monobenzone)

HQ, Hydroquinone

# Summary

## Introduction

Vitiligo is an acquired depigmenting disorder affecting 0.5% of the world population, without sex or racial differences. It affects all age groups (1,2). The etiopathogenic mechanisms of the disease are still poorly understood, and this has held back progress in diagnosis and treatment. Up until now, treatment guidelines have existed at national levels, but no common European viewpoint has emerged. This guideline for the treatment of segmental (SV) and non segmental (NSV) vitiligo has been developed by the members of the Vitiligo European Task Force (VETF) and other colleagues. It summarizes evidence-based and expert-based recommendations (S1 level).

The consensus definition given to generalized/vulgaris or NSV by the VETF is the following (1): *vitiligo vulgaris/NSV is an acquired chronic pigmentation disorder characterized by white patches, often symmetrical, which usually increase in size with time, corresponding to a substantial loss of functioning epidermal and sometimes hair follicle melanocytes.* As it, the definition is not specific enough; thus, it needs to be completed by a list of disorders which may clinically overlap with NSV (the acquired generalised hypomelanoses), but which are clearly attributable to known etiologic factors. In case the diagnosis of vitiligo is uncertain, additional non-invasive and invasive procedures may be needed (Table 1).

SV is defined descriptively as for NSV except for a unilateral distribution («asymmetric vitiligo») that may totally or partially match a cutaneous segment (e.g dermatomal-like), but not necessarily. The term focal is preferred for a limited lesion i.e. where the affected patch is small (10–15 $cm^2$) without an obvious distribution pattern. Other distribution patterns of SV can be encountered that cross several dermatomes or correspond to large areas delineated by Blaschko's lines. Some specific features of SV exist such as rapid onset and hair follicle pigmentary system involvement. One unique segment is involved in most patients, but two or more segments with ipsi- or contralateral distribution are involved in rare patients (Table 2).

Concerning therapy and NSV topographic subtypes, acral lesions show the worst response rate (3). Distinction between SV and NSV may affect prognosis in terms of size of the area to be treated and of resistance of vitiligo to repigmentation. SV runs a protracted course with generally little change after the first year. NSV is less predictable in its course, but is usually slowly progressive over time with episodes of exacerbation. Other forms of vitiligo (such as mucosal or eyelid vitiligo) may necessitate specific approaches not detailed in depth in this guideline.

In terms of therapy, the immune-mediated inflammatory phase of vitiligo needs to be better defined in order to develop specific approaches targeted to this important stage of the disease. At present, there is no convenient marker of this phase, which is mostly silent and only revealed when skin biopsies are taken at the margins of progressing lesions. The rapid clinical progression of vitiligo is frequently considered as the evidence of an inflammatory phase. Stable vitiligo needs a different therapeutic approach in order to regenerate the loss of pigment cells from precursors located in the hair follicle or inter-follicular areas.

In the assessment of a patient with vitiligo it is important to consider age, pre-existing diseases, in particular autoimmune disorders, previous medications, extent, stage and activity of the vitiligo (Table 3), and the patient's perceived severity (4,5,6). Once these factors have been taken into account, a management plan can be proposed. As the care of patients with vitiligo often extends over a long period of time, patients are frequently frustrated by the failure of previous treatments. Psychological stress is common. The treatment plan should be discussed with the patient in order to obtain a high level of compliance. It must be remembered that some therapies are not licensed for vitiligo and can only be prescribed"off-label''(6).

Prior to initiating therapy associated autoimmune disorders, especially thyroid disease, should be excluded. If the patient´s history or routine laboratory parameters suggest additional autoimmune disorders, further investigations and specialist advise (e.g in case of autoimmune polyglandular syndrome) are strongly suggested (Table 1).

## Interventions

### Topical corticosteroids

Topical corticosteroids (TCS) have been applied in the treatment of vitiligo since their introduction in dermatology in the 1950s for their anti-inflammatory and immunomodulating effects. As first-line treatment for limited forms of vitiligo TCS and topical calcineurin inhibitors (TCI) are now widely used (7).

Efficacy

TCS have the best results (75% of repigmentation) on sun-exposed areas, like face and neck (8,9), in dark skin (10) and on recent lesions (11). Acral lesions respond poorly. In a meta-analysis on non-surgical therapies in vitiligo (8) a modest, but significant effect was shown with a success rate of 33 % (16/48) versus 0 % (0/48) in the placebo groups (8). No differences in efficacy were found between clobetasol versus tacrolimus (12), and between clobetasol (13) or mometasone (14) versus pimecrolimus though TCI might be less effective for extra-facial lesions. There is still moderate evidence for the use of TCS, but when used short-term they appear to be safe and effective treatment for both children and adults (7).

Local side-effects are well-known as TCS have been used for several skin disorders for more than half a century. In vitiligo patients treated with potent or very potent TCS these side-effects such as skin atrophy, telangiectasia, hypertrichosis, acneiform eruptions and striae have been observed. Lower potency classes of TCS and newer class III TCS such as mometasone furoate and methylprednisolone aceponate are largely devoid of these side effects.

There are currently no studies available on optimal duration of TCS therapy and on discontinuous applications that could be of help in improving the therapeutic index (7).

**Expert recommendations**

In children and adults who need treatment, once daily application of potent TCS can be advised to patients with limited, extra-facial involvement for a period no longer than 3 months according to a continuous treatment scheme, or better according to a discontinuous scheme i.e. 15 days/month for 6 months with a strict assessment of response based on photographs.

Facial lesions can be treated as effectively and with lesser side-effects by TCI.

As potent TCS appear to be at least as effective as very potent TCS the first category should the first and safest choice.
Systemic absorption is a concern when large areas of skin, regions with a thin skin and children are treated for a prolonged time with potent steroids. The choice then would be for TCS with negligible systemic effects like mometasone furoate or methylprednisolone aceponate.

## Calcineurin inhibitors

Since 2002 the beneficial effects of TCI have been reported for patients with vitiligo, particularly in areas where prolonged use of potent corticosteroids is contraindicated (15). Tacrolimus and pimecrolimus are topical ascomycin immunomodulating macrolactams (TIM) and act as calcineurin inhibitors affecting the activation/maturation of T cells and subsequently inhibiting the production of various cytokines, such as TNFa (16). Moreover, the positive modulation of melanocyte migration and differentiation has been described (17).

Efficacy

Only few randomized trials have been published (12,18,19,20,21). Studies show beneficial results mainly in the head and neck region, both in adults and children patients. UV light exposure during TIM treatment may play a synergistic role (22), even if long-term safety studies should be performed prior to extensively apply this combinatory treatment.

Controversy exists about the possibility of TIMs to induce repigmentation on UV protected areas or areas over bony prominences (12,23,24).

Two randomized, double blind, left-right comparative trials showed that tacrolimus offers similar results compared to clobetasol propionate 0.05% in the treatment of children with vitiligo (12,25). One trial comparing pimecrolimus with clobetasol showed that pimecrolimus could be considered as an alternative treatment to the use of a topical steroid (26). In an open randomized study comparing topical pimecrolimus and tacrolimus, Stinco et al have not shown significant differences in efficacy (27). In another open study, Lotti et al have shown slightly higher responses rate in patients treated with tacrolimus alone (61%) than in those treated with pimecrolimus alone (54.6%) (28). Finally, in a case report describing a head-to-head comparison between topical tacrolimus and pimecrolimus, both agents induced repigmentation of pretibial lesions when used under occlusion overnight. Tacrolimus was slightly more effective (88% repigmentation) than pimecrolimus (73% repigmentation) (29).

Data about the most effective treatment scheme using TIM in vitiligo are still missing. Twice daily applications of tacrolimus ointment have shown more efficacy than once (26). Duration of treatment mentioned in the studies ranged from 10 weeks up to 18 months. Information about the minimal or ideal treatment period in vitiligo as well as the usefulness of long-term intermittent use is not available.

Tolerance

The most common reported side effects for TIMs within the first days of treatment are local application reactions such as burning sensation, pruritus and erythema (12,18,19,20,21,22,23). Although rare, transient skin hyperpigmentation has also been reported (30). The association between TIM and UV or sun exposure is not recommended, according to “black box” FDA warning for atopic dermatitis, even if the possible side effects are limited. In any case, long-term studies are reassuring for atopic dermatitis but still lacking for vitiligo which is an off label prescription in most countries.

**Expert recommendations**

Topical immunomodulators can be considered in adults and children with vitiligo as an alternative to topical steroids for new actively spreading lesions on thin skin. The topical safety profile of TIMs is better compared to potent TCS especially concerning risks of skin atrophy. Considering that data from double blind placebo controlled studies are limited, and that TIMs efficacy is not clearly demonstrated on other sites without occlusion, the use of TIMs should be restricted to selected areas, in priority the head and neck region. Twice daily applications are recommended. The treatment should be prescribed initially for 6 months. During this period of treatment moderate but daily sun exposure should be recommended. If effective, prolonged treatment (e.g. longer than 12 months) may be proposed, since side-effects of long-term use of TCI are reassuring in other conditions such as atopic dermatitis.

## Photochemotherapies (PUVA, KUVA)

Photochemotherapy (PUVA) combines the use of psoralens with long wave (320-340 nm) ultraviolet A (UVA) radiation, producing a beneficial effect that cannot be achieved by the two components separately. Psoralens can be given orally or topically (solutions, creams or bath formulations) followed by exposure to UVA. PUVA-induced stimulation of melanogenesis involves the photoconjugation of psoralens to DNA in melanocytes followed by proliferation of melanocytes, increased formation and melanization of melanosomes, increased transfer of melanosomes to keratinocytes, and activation and increased synthesis of tyrosinase via stimulation of cAMP (31,32,33).

## NB-UVB and targeted phototherapies

The introduction of narrowband 311 nanometer UVB (NB UVB) in the early eighties of the last century has evolved into one of the major accomplishments in the field of phototherapy. NB UVB currently represents the phototherapy of choice for active and/or widespread vitiligo. Side effects are less frequent than in PUVA therapy and efficacy is at least equivalent (34,35). Targeted phototherapy devices (Excimer laser or lamp) deliver light in the UVB range (peak at 308 nm) and are particularly suitable to treat localized disease (36).

Efficacy

*Photochemotherapies (PUVA, KUVA)*

Until the advent of NB UVB, oral photochemotherapy has been the first line treatment for adult patients with generalized vitiligo but is nowadays considered as second-line therapy. Repigmentation is noted in 70-80% of patients, but complete repigmentation is obtained in only 20% of patients. Relapse can occurs in 75% of patients 1 or 2 years after cessation of therapy. It is not recommended in children under 10-12 years old because of the increased risk of retinal toxicity. For oral PUVA, 8-MOP (0.6-0,8 mg/kg) or TMP (0.6 mg/kg) is given orally 1-3 hours before exposure to UVA. For 5-MOP the usual dosage is 1.2-1.8 mg/kg. Patients should be motivated to continue PUVA therapy for at least 6 months before being considered recalcitrant to this treatment, and 12-24 months of continuous therapy may be necessary to acquire maximal repigmentation. Darker skin types show maximal responses to PUVA and maximal repigmentation occur in patients achieving erythema grade 2 (34,37,38).

For topical PUVA, a thin coat of 8-MOP cream or ointment at very low concentration (0.001%) should be first applied 30 minutes before UVA exposure, with possible further increments in concentration. The advantage of topical therapy is the need for fewer treatments and considerably smaller cumulative UVA doses, as well as lower plasmatic levels and consequently less systemic and ocular phototoxicity (39). The main disadvantages are severe blistering reactions, perilesional hyperpigmentation and lack of effectiveness in limiting the progression of actively spreading vitiligo.

Another photochemotherapy regimen for vitiligo consists of khellin as the photosensitizer, a furanochrome extracted of the plant *Amni visnaga* (5,8 dimetoxi.2 methyl-4,5 furo-6,7 chromone), and UVA irradiation (KUVA) (40,41). The main advantage is its lack of phototoxicity making it safe for use as a home treatment or treatment with natural sun light, even on a daily regimen. It is also less mutagenic than psoralens and it promotes less darkening of normal skin. Khellin can be given orally at 100 mg 2 hours before treatment. The efficacy rate of this treatment can be compared to PUVA, but is limited because approximately 30% of patients present liver toxicity (cytolysis). Khellin can also be formulated for topical applications in a moisturizing cream or carbopol gel at a concentration of 3 to 5%. Systemic KUVA is nowadays largely abandoned. Topical “KUVA-sun” is still sometimes used in sunny countries where there are several months for receiving low doses of natural sunlight; however, its efficacy in comparison with oral PUVA or other therapeutic modalities has not been established.

*NB UVB total body and targeted therapies*

NB UVB phototherapy is easy to perform but a proper dosimetry is mandatory to achieve optimum treatment results. In terms of photosensitivity, patients with vitiligo have traditionally been regarded as skin type I and consequently were treated with very low initial NB UVB doses ranging from 150 to 250 mJ/cm$^2$ to avoid excessive sunburn reactions. However, MED values in vitiligo skin are on average only 35% (95% CI = 31-39%) lower than in normal skin of the same individual, suggesting photodaptation. The erythemal sensitivity in vitiligo patients depends on the skin phototype with darker types tolerating higher UVB doses than subjects with a fair complexion (42,43,44,45,46). Treatment is usually given twice or three times weekly and is continued as long as there is ongoing repigmentation. The extent of disease and the disease activity at onset of treatment do not seem to have an effect on the likelihood of repigmentation.

The majority of comparative studies have shown that NB UVB is more effective than other phototherapeutic modalities. A randomized, double-blind trial confirmed the higher efficacy

of NB UVB versus oral PUVA (8-MOP or 5-MOP) in 50 patients with NSV. Treatment was given twice weekly and assessments were performed every 16 sessions. At the end of the study, the PUVA group had received a mean number of 47 treatments as opposed to 97 treatments in the NB UVB group. Sixty four percent of patients in the NBUVB group had 50% improvement or more compared with 36% of patients in the PUVA group. Moreover, among the patients with more than 48 sessions of treatments, the reduction of depigmented surface area was significantly greater for NB UVB than for PUVA. The color match of repigmented skin was excellent in all patients treated with NB UVB but in only 44% of those treated with PUVA. The conclusion of this study was that NB UVB is superior to oral PUVA in NSV, and therefore, most treatment centers nowadays consider NB UVB phototherapy as the first line treatment for NSV (38). Moreover, 5-MOP is currently unavailable further limiting the use of PUVA therapy. Only few long-term follow-up studies have investigated the persistence of repigmentation after discontinuation of NB-UVB treatment. These studies have shown relapse rates of 21% and 44% within 1 year, and 55% within 2 years, respectively.

Recently, efforts have been made to develop therapeutic devices that deliver high fluency light, laser or incoherent, selectively to the lesions (47,48,49,50,51). Therefore the lesions can be selectively treated while the normal skin is spared. Other known advantages, particularly when using high energetic monochromatic light sources, include rapid induction of repigmentation and the requirement of fewer treatments to achieve repigmentation as compared to conventional NB UVB phototherapy. A recent study demonstrated the greater efficacy of the 308 nm excimer laser treatment over NB UVB phototherapy in producing a more rapid and intense repigmentation (51).

Tolerance

The long term risk of skin cancer is well established for PUVA, which makes it a second line option when NB UVB is not available.

NB UVB, as well as targeted UVB phototherapies, are well tolerated. The most common acute adverse reaction is UV-induced erythema in vitiliginous skin, which is both skin type and UV dose dependent. UVB-induced erythema usually occurs 12-24 h after irradiation and continues within another 24 hours. Since patients are not treated on consecutive days erythema induced by the last UVB exposure usually disappears before the next treatment session. Thus is essential to ask the patient whether, and to what extent they have developed erythema in response to the previous irradiation. A slight erythema reaction in lesional skin is generally considered a good guideline for adequate dosimetry. Higher

therapeutic doses are commonly applied when treating lesional skin only with targeted phototherapies. Therefore, erythema reactions may occur more often and with greater intensity than with NB UVB phototherapy. However, these reactions are confined to small areas of the treated skin and do not impair the general well-being of the patient.
Until now, data supporting the safety of phototherapies in childhood are limited, and caution is recommended.

**Expert recommendations**

Photochemotherapies (PUVA, KUVA)

Oral PUVA is nowadays used in adult patients with generalized vitiligo as a second line therapy. Compared to NB UVB it has the disadvantage of lower efficacy and higher short- and long-term risks. As with NB UVB, 12 to 24 months of continuous therapy may be necessary to acquire maximal repigmentation. For topical PUVA, psoralens should be formulated in creams at very low concentration.

Oral KUVA has been largely abandoned due to significant liver toxicity. Topical khellin might be combined with artifical UVA irradiation or exposure to natural sunlight. However, randomized controlled studies assessing the efficacy of this approach are lacking.

NB-UVB and targeted phototherapies

NB UVB is indicated for generalized NSV. Total body treatment is suggested for lesions involving more than 15-20% of the body area. The total NB UVB has been also considered as treatment for active spreading vitiligo, even if limited supportive data are available. Targeted phototherapies (laser and non laser) are indicated for localized vitiligo and in particular for small lesions of recent onset and childhood vitiligo, to avoid side effects due to total body irradiation with UVB, and in all cases where contraindications exist for total body irradiation with conventional NB UVB (risk for melanoma or non melanoma skin cancer, photo-aggravated disease, etc.).

There is as yet no consensus as to the optimum treatment duration of NB UVB or targeted phototherapy. Many therapists tend to stop irradiation if no repigmentation occurs within the first three months of treatment or in case of unsatisfactory response (less than 25% repigmentation) after 6 months of treatment. Phototherapy is usually continued as long as there is ongoing repigmentation or over a maximum period of one to two years. Maintenance irradiation is not recommended but regular follow-up examinations are suggested for detecting relapse.

## Combination treatments

An increasing numbers of reports indicate the usefulness of combination treatments for vitiligo. These treatments target the immune system, melanocyte proliferation/differentiation, or redox status. The use of combined approach may reduce the potential side effects of each treatment, improving the overall effectiveness and the time needed to achieve repigmentation.

Efficacy and tolerance

A prospective, randomized, controlled, left-right comparison study, showed that the combination of UVA and topical fluticasone propionate was more effective that UVA or topical steroid alone (9). Combining the 308 nm excimer laser with topical hydrocortisone 17-butyrate cream showed significantly higher repigmentation than the laser alone in prospective trial performed for resistant head and neck vitiligo lesions (52).

The efficiency of 308 nm excimer combined with tacrolimus ointment was greater compared to laser treatment alone (21). Tolerance was good and side-effects were limited to constant erythema and, rarely, bullous lesions. These encouraging results have been corroborated by others reports for the combination of UVB light and topical tacrolimus (53). More recently, a synergistic effect for the combination of topical tacrolimus with NB UVB was reported (54,55). Combination of pimecrolimus and NB UVB also appears promising (56). However, the possible increased risk of skin cancers promoted by the association of two immunosuppressive treatments needs to be taken into consideration. Caution is thus recommended before embarking on longer term protocols, and registries of treated patients would be helpful.

The use of calcipotriol with natural sunlight or PUVA has provided some interesting evidence of repigmentation. However, the efficacy of this combination has not been clearly established and data are still controversial (57,58,59). Calcipotriol treatment used with 308 nm excimer laser was recently evaluated in a short prospective study (60). The results show that the addition of topical calcipotriol does not increase the efficacy of the 308 nm excimer laser. Calcipotriol in combination with corticosteroids improved the onset, the degree and the stability of the repigmentation in childhood vitiligo (61).

The combination of topical pseudocatalase with UV has shown very promising results in a pilot non randomised control trial: complete repigmentation on the face and the dorsum of the hands was seen in 90% of patients. Two subsequent studies, failed to confirm the efficacy of pseudocatalase in conjunction with NB UVB (62,63).

Oral antioxidant supplementation was reported to increase the effectiveness of UVB phototherapy in two prospective double-blind placebo-controlled studies (64,65). However, the difference was small and, in one report, was only observed in a subgroup of patients. Thus, larger studies are required to confirm the efficacy of oral antioxidants combined with phototherapy.

Addition of PUVA after surgical treatment enhances the repigmentation rate of vitiligo patches (66,67). The combination of NB-UVB with surgical therapies has been les extensively studied but also enhances repigmentation. A prospective, randomized, double blind study clearly showed that autologous transplanted epidermal cell suspensions followed by NB UVB or PUVA was clearly superior to phototherapy alone for repigmenting vitiligo (68). No direct comparison between NB UVB and PUVA, as a synergistic agent for surgical grafting, is presently available.

In a prospective study, the combination of punch grafting with a topical steroid (flucinolone acetonide 0.1%) has been shown to be as effective as punch grafting followed by PUVA (69). More recently, open studies and case reports have suggested that low doses of oral steroids might be beneficial in addition to surgical procedures.

Low-dose azathioprine (at the maximal dosage of 50 mg/day) in combination with PUVA vs. PUVA alone was evaluated in a randomized trial of 60 NSV patients (70). The mean total repigmentation after 4 months of therapy was higher in the patients who received azathioprine plus PUVA (58,4%) compared with PUVA alone (24,8%). Nausea was reported as side effect in 2 patients.

Finally, in a prospective study of 50 patients, Anbar et al concluded that prior use of ER:YAG laser skin ablation, followed by 5FU application may improve the outcome of short-term NB UVB therapy (71).

**Expert recommendations**

Topical steroids and phototherapy: the anti-inflammatory properties of the steroids may act on the immune/inflammatory component, mainly in recent and active lesions, lowering the total amount of administrated UV. Although prospective studies are still lacking, the combination of TCS and UVB sources (NB UVB and 308 nm excimer lasers or lamps) may be promising for difficult-to-treat areas, e.g. over bony prominences. Potent topical steroids applied once a day (3 weeks out of 4) can be used on vitiligo lesions for the 3 first months of phototherapy.

TCI and phototherapy: There is good evidence that the combination of TCI and UV is effective and provides better results than the two treatments used alone. Although increasing data suggest that the combination of UV and topical TCI is safe, long term data on carcinogenicity are still lacking.

Vitamin D analogues and phototherapy: the use of vitamin D analogues in combination to UV is not recommended as the benefit of the combination therapy appears to be at best very limited.

Phototherapy and other treatments: the antioxidant supply may act by restoring the intracellular redox status, intrinsically and UV-compromised. The association of phototherapy and oral antioxidants might be beneficial but the preliminary results have to be confirmed before such a combination can be recommended.

Phototherapy after surgery: there is now a good level of evidence that phototherapy (NB UVB or PUVA) should be used for 3 or 4 weeks after surgical procedures to enhance repigmentation.

## Oral steroids and other immunosuppressants

### Oral steroids minipulse therapy

Though topical steroids are used extensively in the management of vitiligo, studies on systemic steroids have been sparingly reported in the literature. Pulse therapy refers to the administration of large (supra-pharmacologic) doses of drugs in an intermittent manner to enhance the therapeutic effect and reduce the side effects of a particular drug. Oral minipulse (OMP), i.e. intermittent administration of moderate doses of betamethasone/dexamethasone, has been pioneered in India by Pasricha et al (72) in vitiligo and subsequently in other dermatoses. Systemic steroids can arrest the activity of the disease, if they are used in sufficient doses for a sufficient period of time (72,73,74,75,76). They are in general not effective in repigmenting stable vitiligo. Moreover side effects associated with long- term use of daily systemic corticosteroids may act as deterrent against their common use. In the first reported studies on OMP in vitiligo by Pasricha et al (73,74), betamethasone/ dexamethasone was given as a single oral dose of 5 mg on 2 consecutive days per week. In adults who did not respond to the standard dose of corticosteroids, the dose was increased to 7.5 mg/day and then reduced to 5mg/day when disease progression was arrested. Within 1-3 months of treatment, 89% patients with progressive disease stabilized, while within 2-4 months, repigmentation was observed in 80% of the total patient cohort. The area of repigmentation continued to progress as treatment continued, though none of the patient achieved complete repigmentation. Radakovic-Fijan et al (74), used a dexamethasone minipulses of 10 mg/ day on two consecutive days/week for a maximum period of 24 weeks. Disease activity was arrested in 88% of patients with progressive disease after an average treatment period of 18.2 weeks. Side effects were observed in 69% patients, which included weight gain, insomnia, agitation, acne, menstrual disturbances, and hypertrichosis. Plasma cortisol and corticotrophin levels, though markedly decreased after one pulse, returned to normal before starting the next pulse.

Overall, OMP with either betamethasone or dexamethasone can arrest the progression of vitiligo. However, OMP are not usually suitable alone for repigmentation of vitiligo lesions. In patients with fast spreading vitiligo, phototherapy is usually commenced after this intervention. However, there are no RCT confirming that either speed or magnitude of response to phototherapy and photochemotherapy in patients with generalized fast spreading vitiligo might be potentiated by concomitant administration of oral corticosteroid pulses.

**Expert recommendations**

OMP therapy is considered as not useful to repigment stable vitiligo. Week end OMP starting with low doses (2.5 mg/day) of dexamethasone for fast spreading vitiligo can be considered with a good tolerance profile. The benefit of adding OMP to phototherapy at onset of treatment in progressive vitiligo is not proven and needs further assessment. Optimal duration of OMP therapy to stop vitiligo progression is situated between 3 and 6 months.

## Other immunosuppressants and biologics

Immunosuppressants other than oral steroids have been evaluated in a limited number of studies. Anecdotal reports also exist on the off-label use of some immunomodulating biologics in vitiligo.

*Cyclophosphamide*

Cyclophoshamide (2 x 50 mg/day) was assessed in a small case study of 33 patients with NSV. In 29 patients some repigmentation was seen including acral sites (77). Side effects included hair loss, cytopenia and nausea. Quality of life was not recorded and further details of this case study are not available.

*Cyclosporine*

Systemic cyclosporine (6 mg/kg/day) was tested in 6 patients with NSV (78). Little or no repigmentation was seen in 5 out of 6 patients after several months of therapy. Detailed information of the treated patients is not available. Most prominent side effects were renal dysfunction and hypertension.

*Anti-TNF-α*

A case study assessed the therapeutic potential of etanercept in a small open-label pilot study of 4 patients with non-segmental progressive vitiligo (79). 50 mg Etanercept was given weekly for 12 weeks s.c. followed by 25 mg weekly for a further 4 weeks period. Although tolerability was good none of the patients had a repigmentation response. In another case report (80), a patient with ankylosing spondylitis and progressive NSV was treated with infliximab (350 mg infliximab i.v. in weeks 0, 2 and 6, and then every other weeks for 10 months). After 6 months, spreading of vitiligo stopped and partial or complete repigmentation occurred on several spots. However, it should be noted that NSV may be induced by anti-TNF-α agents (81).

**Expert recommendations**

Current data do not provide enough evidence to recommend any of the above immunosuppressives or biologics in patients with vitiligo. Moreover, the potential side effects of these agents do not justify their use in vitiligo.

### Other systemic interventions: antioxidants

The occurrence of cellular oxidative stress during the progression of vitiligo has been used as a rationale for the topical or systemic administration of antioxidants (82). Pseudocatalase, vitamin E, vitamin C, ubiquinone, lipoic acid, *Polypodium Leucotomos*, catalase/superoxide dismutase combination, *G biloba* are the antioxidants which have been used alone or, more frequently, in combination with phototherapy. The administration of antioxidants during or before phototherapy aims to counteract the oxidative stress induced by UV itself, increasing its effectiveness.

Efficacy

Several open trials suggested that oral or topical administration of single or multiple antioxidants stopped the progression of the disease and promoted repigmentation (83). RCT reported so far suggest that vitamin E is effective for the recovery of skin lipid peroxidation induced by PUVA treatment (84); a mixture of a-lipoic acid, vitamin E and C, administrated in a double-blind placebo controlled trial, promotes reduction of UV dosage together with improvement of the repigmentation (64);*Polypodium leucotomos*, characterized by antioxidant, photosensitizing and immunomodulatory activities, is effective when used in association with PUVA or UVB (65);*Gingko biloba*, containing polyphenol compounds with anti-inflammatory, immunomodulatory, and anti- oxidant activities appears also to have promising results. However, in reported studies, questions arised due to the limited number of enrolled patients and inconsistent outcome parameters (85,86,87). No side effects have been reported until now but long term administration has raised concerns (88).

**Expert Recommendations**

Antioxidant supplementation could be useful during UV therapy, and during the reactivation phase of vitiligo  However, RCTs evaluating systemic antioxidant supplements provide a limited evidence of efficacy, and further confirmation. Is needed before recommending their prescription in vitiligo.

## Surgery

Surgical procedures aim to replace the melanocytes that are missing in the achromic areas with melanocytes obtained from a normally pigmented autologous donor site. Several melanocyte transplantation techniques can be performed under local anesthesia in an outpatient facility. However, transplantation for extensive areas of vitiligo may require general anesthesia and a fully equipped operation theater. All methods requires surgical training and should be performed under strict sterile conditions (89,90,91,92,93,94,95,96).

*Techniques*

1. Punch grafting (tissue graft) is the easiest and less expensive one, but it is not suitable for large lesions and seldom gives even repigmentation.
2. Epidermal blister grafting gives excellent cosmetic results, but this procedure is time consuming and large areas cannot be treated.
3. Ultra-thin epidermal sheet grafting can treat larger areas (up to 200cm2) but requires skill and experience.
4. Cellular grafts consist of a basal cell layer autologous suspension containing melanocytes and keratinocytes. It provides the advantage that a given area can be treated with a good donor: recipient ratio ranging from 5 to 10 folds. Initially, this procedure required a laboratory facility for cell processing and a trained dermatologist but single-use kits for enzymatic separation of thin shaving biopsies from the graft area have been developed. Here, a cell suspension can be easily generated even in the operating room within less than 1 hr.
5. Transplants of pure cultured melanocytes expanded in vitro can treat lesions up to 500cm$^2$. This method is more expensive, time consuming and requires specialized staff.

*Side effects*

The highest incidence of adverse events occurs with punch grafting (scar formation at the donor site, cobblestoning of the acceptor area) followed by ultra-thin epidermal grafting (transient or permanent hypopigmentation, hypertrophic scars on the donor site, milia formation on the recipient site) and suction blister epidermal grafting (transitory hyperpigmentation on donor site, imperfect color matching on the recipient site) (92). Rare adverse events have been observed with cellular grafting such as temporary depigmentation at donor site and transitory inflammatory hyperpigmentation at recipient site. With a right choice of the method depending on the anatomical location and size of

the lesions the side effects can be minimized and follow-up studies have documented long-term stability and safety (91).

*Indications*

Although surgery is normally indicated for all types of stable vitiligo, only a small number of vitiligo patients are suitable for melanocyte transplantation. The best indications are stabilized segmental or focal vitiligo. In generalized vitiligo various recommendations suggest a period of disease inactivity ranging from six months to two years, and absence of history of Koebner's isomorphic response. No consensus exists concerning the minimal age for surgery which is generally performed under local anesthesia (89,92,93,94). Although surgical management of the achromic areas is a fast and effective way of repigmenting vitiligo, it has to be stressed that the treatment do not change the overall prognosis of the disease in case of NSV. When a surgical treatment is conducted in NSV it should be combined with other medical and or UV-light treatment for best outcome and long-term stability,.

**Expert recommendations**

Surgery option should be reserved for patients with SV and other localized forms of vitiligo, after the documented failure of medical interventions. For NSV, patients with stable form of the disease and negative history of Koebner phenomenon are eligible, but the risk of relapse must be explained thoroughly to the patient.

## Other interventions

### Camouflage

Considering the impact of the disease on the patient's self-body image, camouflage techniques are an important part of the global management of the disease (96,97,98,99,100). Products developed to disguise aesthetic skin disfigurement, require specialized application techniques. There are many ways to conceal small or large areas of vitiligo which can increase the patient's confidence and improve quality of life (96). Among products, there is a wide choice of self-tanners, stains, dyes, whitening lotions, tinted cover creams, compact, liquid and stick foundations, fixing powders, fixing sprays, cleansers, semi-permanent and permanent tattoos, dyes for pigmenting facial and scalp white hairs (99). Permanent camouflage, micropigmentation and tattoos should be considered with particular caution (100), due to the unpredictable course of the vitiligo.

**Expert recommendations**

Self-tanners in gel, cream, lotion or spray, give to the skin a brown color that resembles a natural tan and normally lasts from three to five days can be used throughout the year, are waterproof and the fake tan developed does not stain clothes or sheet. Unluckily, sea water makes them fade away quickly, while swimming pool water does not..

Highly pigmented cover creams are lightweight, easy to apply, and almost always free of fragrance. Their waterproof characteristics allow shower and swimming. On the face, they should be applied and removed every day. A fixing spray is available to maintain the corrective make-up for a whole day. Make up removers are necessary to clean the skin, with gentle and delicate movements to avoid koebnerization.

Dermal pigmentation, cosmetic tattoos. Cosmetic tattoo may be suitable for depigmented lips, especially in black people, and for depigmented nipples. In other vitiligo areas, caution is recommendable.

## Depigmentation

In patients with extensive and refractory vitiligo, depigmenting the remaining islands through chemical or physical methods of normal skin may a cosmetically acceptable option. Monobenzone ethyl ester (MBEH) is a derivative of hydroquinone (HQ). Unlike HQ, MBEH almost always causes nearly irreversible depigmentation of the skin (101,102).
The patients with the highest phototypes (V and VI), for which the contrast between dark pigmented skin and white vitiligo areas is actually disfiguring, may be the best candidates. However, patients with phototypes I and II may also obtain better cosmetic improvement using depigmenting agents than with repigmenting regimen on exposed areas.
Considering that most approaches lead to an irreversible depigmentation, the patients must be extensively informed.
MBEH is applied topically as a 20% cream. A thin layer of cream should be applied uniformly and rubbed into the pigmented area 2–3 times daily. Prolonged exposure to sunlight should be avoided during treatment, or a sunscreen should be used, as exposure to sunlight reduces the depigmenting effect of the drug. Depigmentation is usually obtained after 1–4 months of treatment. After 4 months of treatment without success, the drug should be discontinued. When the desired degree of depigmentation is obtained, monobenzone should be applied as often as needed to maintain depigmentation (usually only 2 times weekly) (102).
Mild transient skin irritation or sensitization causing eczema may occur following topical application of monobenzone. Although these reactions are usually transient, the treatment should be discontinued if irritation, burning sensation, or dermatitis occurs. Ocular side effects have been rarely reported. Areas of normal skin distant to the site of monobenzone application have become depigmented. Monobenzone has been proposed in association with retinoic acid in order to overcome the resistance to treatment (103).
The Q-switched 755-nm ruby laser has been proposed as an alternative to induce persistent depigmentation (104). It can be used alone or in combination with methoxyphenol (105,106). It has been reported to be able to destroy melanin and melanin-bearing cells. Cryotherapy has been reported as an unexpensive depigmentation therapy, but due to the risk of scaring, it should only be used by experienced dermatologists(107,108,109). However, due to limited published information, the exact place of this intervention needs further evaluation. Overall, comparative clinical trials are needed to compare the efficacy of various depigmentation methods (107).

**Expert recommendations**

Only patients with extensive disfiguring vitiligo should be treated and only after exploring other possible therapies. The patient should be advised that monobenzone is a potent depigmenting agent and not a cosmetic skin bleach. Depigmentation can be also obtained by Q-switched ruby laser, alone or in combination with methoxyphenol.

## Psychological interventions

Vitiligo is a common pigmentary disorder that does not lead to severe physical illness, nevertheless patients experience a variable degree of psychosocial impairment (110). Depigmentation exerts a negative impact on the patient's appearance and self-esteem. Most vitiligo patients find their disfigurement moderately or severely intolerable, and suffer from poor body image, low self-esteem and social isolation in both personal and professional relationships. Levels of disability vary according to objective factors such as the extension and site of the disease, phototype, ethnicity and cultural background (112,113). The prevalence of psychiatric morbidity associated with vitiligo ranges from 25% to 30% in Western Europe, with prevalent fair skinned subjects, and from 56% to 75% in India, with a predominance of dark skinned patients (114).

In addition to objective factors, subjective factors have been demonstrated to be important in the psychological impact of vitiligo. Perceived severity of the disease is more influenced by the patient's personality than by objective traits of vitiligo (114).Additional discomforting aspects are the chronic, unpredictable nature of the disease and the lack of a universally effective treatment (111).

**Expert recommendations**

Subjective assessment should be included as part of the evaluation of disease severity using an analog scale with the question: "How much does your skin disease bother you currently?" or a QoL questionnaire such as the DLQI. If possible, a psychologically oriented interview is further recommended in order to evaluate the perceived influence of the disease and to identify patients for which the psychological support may be useful.

In the case of a recognized psychosocial impairment, different types of psychological interventions can be proposed. So far, no specific psychological therapeutic intervention prevails based on published evidence.

Patients appreciate the opportunity to express difficulties related to their disease and to be understood and listened to. This is particularly relevant in the case of adolescents or dark-skinned individuals with experiences of stigmatization related to cultural background. In this case, besides individual psychosocial therapeutic interventions, community interventions can be necessary.

## Summary and treatment algorithms

### Limitations

Given the importance of charlatanism in the vitiligo field, counselling patients to avoid some therapies of dubious efficacy is indeed a major step. As stated in the vitligo Cochrane review (6), there are many limitations to derive a valuable algorithm of treatment for all vitiligo patients based on RCTs. First, RCT are rare and often lacking important methodological steps or details. Second, studies have often been conducted in heterogeneous groups in terms of vitiligo duration or progression, if not mixing localized, segmental and nonsegmental forms. Third, confounding factors are many, e.g. light exposure in long term interventions for which light sources may influence outcome, nutritional intake if antioxidant status is considered, or awareness on limitation of the Koebner's phenomenon which is rarely taken into account.

### Stepwise approach

Nevertheless, a stepwise treatment approach divided by type of vitiligo and extent, which needs modulation by visibility, age and coping is outlined in Table 4 and algorithm. A zero line is always possible, meaning no treatment if the disease is not bothering the patient. The environmental factors (occupation, Koebner's phenomenon, sustained stress or anxiety) should be always discussed in the management plan. For SV, triggering neurogenic factors are usually envisaged but good studies are lacking to prove this point. This stepwise approach should be considered as a proposal based mostly on EBM data. However, there is much room for modulation and innovation based on this scheme (115).

### Perspectives

For a common disorder like vitiligo, there are probably subtypes in terms of mechanisms of melanocyte loss. The background in generalized vitiligo is polygenic and multifactorial and this should be reflected in more personalized approaches in the future (115). We still do not know if cutaneous inflammation, which seems more common than previously envisaged in progressive disease is a shared feature in all cases. If it is the case, a more aggressive anti-inflammatory therapy would probably be helpful, and there is clearly a need to assess more precisely the use of systemic immunosuppressants in this group. It is surprising that a drug widely used in other chronic inflammatory skin disorders such as methotrexate have not been yet tested in a RCT. If the initial step preceding inflammation comes from a local predisposition of melanocytes to attach poorly to the basement

membrane, there are possible targets to improve adhesion mechanisms, but a more precise description of the basic impairment is obviously needed. The issue of self renewal (stemness) aptitude of melanocytes has been raised especially for SV (115), which clearly benefits from autologous grafting  If some vitiligo cases are due to the impairment of melanocyte survival mechanisms, growth factor supplementation, such as MSH analogs already tested in protoporphyria (116) could be used. Survival impairment due to a defect of the cellular environment i.e. keratinocytes,  as suggested by Bondanza et al, may offer new therapeutic perspectives (117). Improving, in a symptomatic approach, the antioxidant status of the epidermis has been attempted, but more powerful tools using gene transfer might be used in the future (118).

When melanocyte loss has been stopped, therapy needs to address repigmentation. New repigmenting therapies are emerging such as He-Ne lasers and prostaglandin E2 (119,120). Recent development in the field of melanocyte precursors in the hair follicle are promising. If we can better stimulate the emigration of those cells towards the epidermis and understand why they usually stop migrating when becoming pigmented, a major step would be achieved. There is also the issue of dormant residual (de-differentiated) melanocytes which could be resuscitated in interfollicular zones and opening some new therapeutic avenues. Surgical treatments for limited and disfiguring disease have dramatically improved in the last 20 years. Newer technologies derived from progenitors or reprogrammed skin cells (121)  will probably further increase our possibilities of surgical intervention.

**Disclaimer**

These guidelines are defined for dermatologists in the clinic and in private practice. Furthermore, they are meant to serve as an aid for health insurance organizations and political decision- makers.

The experts restricted the attention to aspects and approaches that they felt were especially relevant. Steps that can be considered part of every physician’s general obligations when prescribing drugs (inquiring about allergies and intolerance reactions, as well as identifying potential contraindications) are not reported. Moreover, it was considered obvious, and not declared, to inform all patients about the specific risks associated with any given systemic therapy.

During the preparation of this Guideline, further clinical and experimental studies have been surely carried out, proving or counteracting the Guideline. Consequently, the authors can take no responsibility for dosage or treatment decisions taken in this rapidly changing

field. The authors and the publishers kindly request that readers inform them of any inaccuracies they may find.

As with all fields of scientific inquiry, medicine is subject to continual development, and existing treatments are always changing. Great care was taken while developing these guidelines to ensure that they would reflect the most current scientific knowledge at the time of their completion. Readers are nevertheless advised to keep themselves abreast of new data and developments subsequent to the publication of the guidelines.

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**Table 1. Recommended diagnostic procedures in vitiligo**

| If diagnosis is certain | If diagnosis is uncertain |
|---|---|
| Anti-TPO, anti-thyroglobulin antibodies<br>TSH and other tests if needed to assess thyroid function or diagnosis (e.g. anti TSH-R antibodies if Graves'disease)<br><br>Additional autoantibodies (only if patient´s history, family history and/or laboratory parameters point to a strong risk of additional autoimmune disease), endocrinologist/immunologist advice if multiple autoimmune syndrome detected. | • Punch biopsy from lesional and non-lesional skin<br>• Others if needed (mycology, molecular biology to detect lymphoma cells…) |

**Table 2: Classification of vitiligo[1]**

| Type of vitiligo | Subtypes | Remarks |
|---|---|---|
| **Non segmental (NSV)** | (Focal)*, Mucosal, Acrofacial, Generalised, Universal. | Subtyping may not reflect a distinct nature, but useful information for epidemiologic studies. |
| **Segmental (SV)** | Focal, Mucosal, Unisegmental, bi- or plurisegmental. | Further classification according to distribution pattern possible, but not yet standardized. |
| **Mixed (NSV+SV)** | According to severity of SV | Usually the SV part in mixed vitiligo is more severe. |
| **Unclassified** | Focal at onset, multifocal asymmetrical non segmental, mucosal (one site). | This category is a meant to allow, after a sufficient observation time (and if necessary investigations), to make a definitive classification. |

*possible onset of NSV

**Table 3. Evaluation check-list for NSV (adapted from references 1 and 2)**

| Patient features | Disease features | Family | Interventions |
|---|---|---|---|
| Phototype<br>Ethnic origin<br>Age at onset<br>Psychological profile<br>Halo nevus<br>history of autoimmune diseases<br>Global QoL assessment (10 cm analog scale) | Duration(patient's opinion: (progressive, regressive, stable over the last 6 months)<br>Previous repigmentation, Koebner's phenomenon<br>Genitals involvement<br>photographs (if possible UV-light photographs) | premature hair graying<br>vitiligo<br>autoimmune disease (family tree) | Type and duration of previous treatments including opinion of patient(list): useful/not useful<br>Current treatment(s)<br>Treatments (list) for other diseases |

**Table 4. General outline of management for vitiligo** (adapted from reference 3).

| Type of Vitiligo | Level | Usual Management |
|---|---|---|
| SV or limited NSV (<2-3% of body surface) | First line | Avoidance of triggering factors, local therapies (corticosteroids, calcineurin inhibitors). |
| | Second line | Localized NB-UVB therapy, especially Excimer monochromatic lamp or laser. |
| | Third line | Consider surgical techniques if repigmentation cosmetically unsatisfactory on visible areas. |
| NSV | First line | Avoidance of triggering/aggravating factors. Stabilization with NB-UVB therapy, at least 3 months. Optimal duration at least 9 months if response. Combination with systemic/ topical therapies, including reinforcement with localized UVB therapy, possible. |
| | Second line | Systemic steroids (e.g. 3-4 month minipulse therapy) or immunosuppressants if rapidly progressing disease or absence of stabilization under NB-UVB. |
| | Third line | Graft in non responding areas especially with high cosmetic impact. However, Koebner phenomenon limits the persistence of grafts. Relative contraindication in areas such as dorsum of hands. |
| | Fourth line | Depigmentation techniques (hydroquinone monobenzyl ether or 4-methoxyphenol alone or associated with Q switch ruby laser) in non responding widespread (> 50%) or highly visible recalcitrant facial/hands vitiligo |

A no treatment option (zero line) can be considered in patients with a fair complexion after discussion. For children, phototherapy is limited by feasibility in the younger age group and surgical techniques rarely proposed before prepubertal age. There is no current recommendation applicable to the case of rapidly progressive vitiligo, not stabilized by UV therapy. For all subtypes of disease or lines of treatment, psychological support and counselling including access to camouflage instructors is needed.

Conflicts of interests : NONE

| The Work Under Consideration for Publication | | | | | |
|---|---|---|---|---|---|
| | | **Name** | **Name** | **Name** | **Name** |
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|---|---|---|---|---|---|
| 1 | Board membership | JACFR Pediatric board Abbott | | | |
| 2 | Consultancy | Galderma, Pierre Fabre | | | |
| 3 | Employment | | | | |
| 4 | Expert testimony | | | | |
| 5 | Grants/grants pending | | | | |
| 6 | Payment for lectures including service on speakers bureaus | Several for Atopic Dermatitis and Psoriasis not Vitiligo (Galderma, Intendis, Astellas) | | | |
| 7 | Payment for manuscript preparation | | | | |
| 8 | Patents (planned, pending or issued) | Issued Propranolol for hemangiomas 2011CEuropean patent | | | |
| 9 | Royalties | | | | |
| 10 | Payment for | Astellas (AD | | | |

| | | | | | |
|---|---|---|---|---|---|
| | development of educational presentations | Workshop 2011) | | | |
| 11 | Stock/stock options | | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | EADV and JDP meeting, Schering Plough, Astellas, Bioderma | | | |
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| 8 | Patents (planned, pending or issued) | | | | |
| 9 | Royalties | | | | |
| 10 | Payment for development of educational presentations | | | | |
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Dr.Agustin Alomar do not receive any fee that means conflict of interest in relation to the material in the guidelines

Barcelona 14th Oct 2011

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| The Work Under Consideration for Publication | | | | | |
|---|---|---|---|---|---|
| | | **Markus Böhm** | **Name** | **Name** | **Name** |
| 1 | Grant | NONE | | | |
| 2 | Consulting fee or honorarium | NONE | | | |
| 3 | Support for travel to meetings for the study or other purposes | NONE | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | NONE | | | |
| 5 | Payment for writing or reviewing the manuscript | NONE | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | NONE | | | |
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| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | NONE | | | |
| 2 | Consultancy | NONE | | | |
| 3 | Employment | NONE | | | |
| 4 | Expert testimony | NONE | | | |
| 5 | Grants/grants pending | NONE | | | |
| 6 | Payment for lectures including service on speakers bureaus | NONE | | | |
| 7 | Payment for manuscript preparation | NONE | | | |
| 8 | Patents (planned, pending or issued) | NONE | | | |
| 9 | Royalties | NONE | | | |
| 10 | Payment for development of educational presentations | NONE | | | |
| 11 | Stock/stock options | NONE | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | NONE | | | |
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Conflicts of interests

Maria Lucia Dell'Anna, MD

| The Work Under Consideration for Publication | | | | | |
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| | | **Name** | **Name** | **Name** | **Name** |
| 1 | Grant | no | No | no | No |
| 2 | Consulting fee or honorarium | no | No | No | No |
| 3 | Support for travel to meetings for the study or other purposes | no | No | No | No |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | no | No | No | No |
| 5 | Payment for writing or reviewing the manuscript | no | No | No | No |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | no | no | No | no |
| 7 | Other | no | no | no | no |

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| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | no | no | no | No |
| 2 | Consultancy | no | no | no | No |
| 3 | Employment | no | no | no | No |
| 4 | Expert testimony | no | no | no | No |
| 5 | Grants/grants pending | no | no | no | No |
| 6 | Payment for lectures including service on speakers bureaus | no | no | no | No |
| 7 | Payment for manuscript preparation | no | no | no | No |
| 8 | Patents (planned, pending or issued) | no | no | no | No |
| 9 | Royalties | no | no | no | No |
| 10 | Payment for development of educational presentations | no | no | no | No |
| 11 | Stock/stock options | no | no | no | no |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | no | no | no | No |
| 13 | Other (err on the side of full | no | no | no | no |

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| 3 | Support for travel to meetings for the study or other purposes | NONE | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | NONE | | | |
| 5 | Payment for writing or reviewing the manuscript | NONE | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | NONE | | | |
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| 1 | Board membership | NONE | | | |
| 2 | Consultancy | NONE | | | |
| 3 | Employment | NONE | | | |
| 4 | Expert testimony | NONE | | | |
| 5 | Grants/grants pending | NONE | | | |
| 6 | Payment for lectures including service on speakers bureaus | NONE | | | |
| 7 | Payment for manuscript preparation | NONE | | | |
| 8 | Patents (planned, pending or issued) | NONE | | | |
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| The Work Under Consideration for Publication | | | | | |
|---|---|---|---|---|---|
| Eleftheriadou | | **Name** | **Name** | **Name** | **Name** |
| 1 | Grant | none | | | |
| 2 | Consulting fee or honorarium | none | | | |
| 3 | Support for travel to meetings for the study or other purposes | none | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | none | | | |
| 5 | Payment for writing or reviewing the manuscript | none | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | none | | | |
| 7 | Other | | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | none | | | |
| 2 | Consultancy | none | | | |
| 3 | Employment | none | | | |
| 4 | Expert testimony | none | | | |
| 5 | Grants/grants pending | none | | | |
| 6 | Payment for lectures including service on speakers bureaus | none | | | |
| 7 | Payment for manuscript preparation | none | | | |
| 8 | Patents (planned, pending or issued) | none | | | |
| 9 | Royalties | none | | | |
| 10 | Payment for development of educational presentations | none | | | |
| 11 | Stock/stock options | none | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | none | | | |
| 13 | Other (err on the side of full disclosure) | none | | | |

* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | none | | | |

Dr VIKTORIA ELEFTHERIADOU

21/12/2011

Conflicts of interests

| The Work Under Consideration for Publication **EDF-Guidelines for Vitiligo** | | | | | |
|---|---|---|---|---|---|
| | | **Khaled Ezzedine** | **Name** | **Name** | **Name** |
| 1 | Grant | NO | | | |
| 2 | Consulting fee or honorarium | NO | | | |
| 3 | Support for travel to meetings for the study or other purposes | NO | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | NO | | | |
| 5 | Payment for writing or reviewing the manuscript | NO | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | NO | | | |
| 7 | Other | NO | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | NO | | | |
| 2 | Consultancy | NO | | | |
| 3 | Employment | NO | | | |
| 4 | Expert testimony | NO | | | |
| 5 | Grants/grants pending | NO | | | |
| 6 | Payment for lectures including service on speakers bureaus | NO | | | |
| 7 | Payment for manuscript preparation | NO | | | |
| 8 | Patents (planned, pending or issued) | NO | | | |
| 9 | Royalties | NO | | | |
| 10 | Payment for development of educational presentations | NO | | | |
| 11 | Stock/stock options | NO | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | NO | | | |
| 13 | Other (err on the side of full | NO | | | |

| | | | | | |
|---|---|---|---|---|---|
| | disclosure) | | | | |

* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | NO | | | |

## Conflicts of interests

| The Work Under Consideration for Publication | | | | | |
|---|---|---|---|---|---|
| | | **Gauthier** | **Name** | **Name** | **Name** |
| 1 | Grant | none | | | |
| 2 | Consulting fee or honorarium | none | | | |
| 3 | Support for travel to meetings for the study or other purposes | none | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | none | | | |
| 5 | Payment for writing or reviewing the manuscript | none | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | none | | | |
| 7 | Other | none | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | none | | | |
| 2 | Consultancy | none | | | |
| 3 | Employment | none | | | |
| 4 | Expert testimony | none | | | |
| 5 | Grants/grants pending | none | | | |
| 6 | Payment for lectures including service on speakers bureaus | none | | | |
| 7 | Payment for manuscript preparation | none | | | |
| 8 | Patents (planned, pending or issued) | Patent for a lightening agent | | | |
| 9 | Royalties | none | | | |
| 10 | Payment for development of educational presentations | none | | | |
| 11 | Stock/stock options | none | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | Invited speaker by dermatological societies | | | |
| 13 | Other (err on the side of full disclosure) | none | | | |

* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | none | | | |

Conflicts of interests David J GAWKRODGER

| The Work Under Consideration for Publication | | | | | |
|---|---|---|---|---|---|
| | | **Name DJ GAWKRODGER** | **Name** | **Name** | **Name** |
| 1 | Grant | NONE | | | |
| 2 | Consulting fee or honorarium | NONE | | | |
| 3 | Support for travel to meetings for the study or other purposes | BASILEA UK<br>JANSSEN PHARMACEUTICALS uk | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | NOVARTIS USA<br>PROCTOR & GAMBLE uk | | | |
| 5 | Payment for writing or reviewing the manuscript | BASILEA UK | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | NONE | | | |
| 7 | Other | NONE | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | EADV FOSTERING TRAINEES BOARD, EADV OFFICE MANAGEMENT TASK FORCE MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AUTHORITY- VICE-CHAIR OF EXPERT ADVISORY GROUP | | | |
| 2 | Consultancy | NO | | | |
| 3 | Employment | Sheffield Teaching Hospitals NHS Foundation Trust | | | |
| 4 | Expert testimony | LAW COURTS ENGLAND | | | |
| 5 | Grants/grants pending | NONE | | | |
| 6 | Payment for lectures including service on speakers bureaus | LEO PHARMACEUTICALS | | | |
| 7 | Payment for manuscript preparation | NONE | | | |
| 8 | Patents (planned, pending or issued) | NONE | | | |
| 9 | Royalties | ELSEVIER, WILEY | | | |
| 10 | Payment for development of educational presentations | CARDIFF UNIVERSITY | | | |
| 11 | Stock/stock options | NONE IN HEALTHCARE AT TIME OF WRITING | | | |

| | | | | | |
|---|---|---|---|---|---|
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | SEE ABOVE | | | |
| 13 | Other (err on the side of full disclosure) | NONE TO MY KNOWLEDGE | | | |

* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | NONE THAT I AM AWARE OF | | | |

## Conflicts of interests

| The Work Under Consideration for Publication | | | | | |
|---|---|---|---|---|---|
| | | **Jouary Thomas** | **Name** | **Name** | **Name** |
| 1 | Grant | None | | | |
| 2 | Consulting fee or honorarium | None | | | |
| 3 | Support for travel to meetings for the study or other purposes | None | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | None | | | |
| 5 | Payment for writing or reviewing the manuscript | None | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | None | | | |
| 7 | Other | None | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | BMS | | | |
| 2 | Consultancy | BMS, Schering-Plough, Roche | | | |
| 3 | Employment | No | | | |
| 4 | Expert testimony | No | | | |
| 5 | Grants/grants pending | No | | | |
| 6 | Payment for lectures including service on speakers bureaus | No | | | |
| 7 | Payment for manuscript preparation | No | | | |
| 8 | Patents (planned, pending or issued) | No | | | |
| 9 | Royalties | No | | | |
| 10 | Payment for development of educational presentations | BMS | | | |
| 11 | Stock/stock options | No | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | BMS, Roche | | | |
| 13 | Other (err on the | | | | |

| | | | | | |
|---|---|---|---|---|---|
| | side of full disclosure) | | | | |

* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | None | | | |

Conflicts of interests: NONE DECLARED

| The Work Under Consideration for Publication | | | | | |
|---|---|---|---|---|---|
| Giovanni Leone | | **Name** | **Name** | **Name** | **Name** |
| 1 | Grant | | | | |
| 2 | Consulting fee or honorarium | | | | |
| 3 | Support for travel to meetings for the study or other purposes | | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | | | | |
| 5 | Payment for writing or reviewing the manuscript | | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | | | | |
| 7 | Other | | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | | | | |
| 2 | Consultancy | | | | |
| 3 | Employment | | | | |
| 4 | Expert testimony | | | | |
| 5 | Grants/grants pending | | | | |
| 6 | Payment for lectures including service on speakers bureaus | | | | |
| 7 | Payment for manuscript preparation | | | | |
| 8 | Patents (planned, pending or issued) | | | | |
| 9 | Royalties | | | | |
| 10 | Payment for development of educational presentations | | | | |
| 11 | Stock/stock options | | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | | | | |
| 13 | Other (err on the side of full disclosure) | | | | |

* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | | | | |

Giovanni Leone MD
Photodermatology Unit
San Gallicano Institute
Via Elio Chianesi, 53
00144 Roma
ITALY

Signed in Rome on November, 14, 2011

## Conflicts of interests

| The Work Under Consideration for Publication | | | | | |
|---|---|---|---|---|---|
| Silvia Moretti | | **Name** | **Name** | **Name** | **Name** |
| 1 | Grant | none | | | |
| 2 | Consulting fee or honorarium | none | | | |
| 3 | Support for travel to meetings for the study or other purposes | none | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | none | | | |
| 5 | Payment for writing or reviewing the manuscript | none | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | none | | | |
| 7 | Other | none | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | none | | | |
| 2 | Consultancy | none | | | |
| 3 | Employment | associate professor at university | | | |
| 4 | Expert testimony | none | | | |
| 5 | Grants/grants pending | none | | | |
| 6 | Payment for lectures including service on speakers bureaus | none | | | |
| 7 | Payment for manuscript preparation | none | | | |
| 8 | Patents (planned, pending or issued) | none | | | |
| 9 | Royalties | none | | | |
| 10 | Payment for development of educational presentations | none | | | |
| 11 | Stock/stock options | none | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | none | | | |
| 13 | Other (err on the side of full disclosure) | none | | | |

* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | none | | | |

Firenze, October 17, 2011

Stefano Bretti

## Conflicts of interests

| The Work Under Consideration for Publication **EDF-Guidelines for Vitiligo** | | | | | |
|---|---|---|---|---|---|
| | | **Ludmilla Krobotova** | **Name** | **Name** | **Name** |
| 1 | Grant | NONE | | | |
| 2 | Consulting fee or honorarium | NONE | | | |
| 3 | Support for travel to meetings for the study or other purposes | NONE | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | NONE | | | |
| 5 | Payment for writing or reviewing the manuscript | NONE | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | NONE | | | |
| 7 | Other | NONE | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | NONE | | | |
| 2 | Consultancy | NONE | | | |
| 3 | Employment | NONE | | | |
| 4 | Expert testimony | NONE | | | |
| 5 | Grants/grants pending | NONE | | | |
| 6 | Payment for lectures including service on speakers bureaus | NONE | | | |
| 7 | Payment for manuscript preparation | NONE | | | |
| 8 | Patents (planned, pending or issued) | NONE | | | |
| 9 | Royalties | NONE | | | |
| 10 | Payment for development of educational presentations | NONE | | | |
| 11 | Stock/stock options | NONE | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | NONE | | | |
| 13 | Other (err on the side of full | NONE | | | |

| | | | | | |
|---|---|---|---|---|---|
| | disclosure) | | | | |

* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | NONE | | | |

## Conflicts of interests

| The Work Under Consideration for Publication **EDF-Guidelines for Vitiligo** | | | | | |
|---|---|---|---|---|---|
| | | **Mats J Olsson** | **Name** | **Name** | **Name** |
| 1 | Grant | NO | | | |
| 2 | Consulting fee or honorarium | NO | | | |
| 3 | Support for travel to meetings for the study or other purposes | NO | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | NO | | | |
| 5 | Payment for writing or reviewing the manuscript | NO | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | NO | | | |
| 7 | Other | NO | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | NO | | | |
| 2 | Consultancy | NO | | | |
| 3 | Employment | NO | | | |
| 4 | Expert testimony | NO | | | |
| 5 | Grants/grants pending | NO | | | |
| 6 | Payment for lectures including service on speakers bureaus | NO | | | |
| 7 | Payment for manuscript preparation | NO | | | |
| 8 | Patents (planned, pending or issued) | NO | | | |
| 9 | Royalties | NO | | | |
| 10 | Payment for development of educational presentations | NO | | | |
| 11 | Stock/stock options | NO | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | NO | | | |
| 13 | Other (err on the side of full disclosure) | NO | | | |

* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | NO | | | |

## Conflicts of interests

| The Work Under Consideration for Publication **EDF-Guidelines for Vitiligo** | | | | | |
|---|---|---|---|---|---|
| | | **Davinder Parsad** | **Name** | **Name** | **Name** |
| 1 | Grant | NO | | | |
| 2 | Consulting fee or honorarium | NO | | | |
| 3 | Support for travel to meetings for the study or other purposes | NO | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | NO | | | |
| 5 | Payment for writing or reviewing the manuscript | NO | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | NO | | | |
| 7 | Other | NO | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | NO | | | |
| 2 | Consultancy | NO | | | |
| 3 | Employment | NO | | | |
| 4 | Expert testimony | NO | | | |
| 5 | Grants/grants pending | NO | | | |
| 6 | Payment for lectures including service on speakers bureaus | NO | | | |
| 7 | Payment for manuscript preparation | NO | | | |
| 8 | Patents (planned, pending or issued) | NO | | | |
| 9 | Royalties | NO | | | |
| 10 | Payment for development of educational presentations | NO | | | |
| 11 | Stock/stock options | NO | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | NO | | | |
| 13 | Other (err on the side of full | NO | | | |

| | | | | | |
|---|---|---|---|---|---|
| | disclosure) | | | | |

* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | NO | | | |

## Conflicts of interests

| The Work Under Consideration for Publication | | | | | |
|---|---|---|---|---|---|
| | | **Passeron** | **Name** | **Name** | **Name** |
| 1 | Grant | | | | |
| 2 | Consulting fee or honorarium | | | | |
| 3 | Support for travel to meetings for the study or other purposes | | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | | | | |
| 5 | Payment for writing or reviewing the manuscript | | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | | | | |
| 7 | Other | | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | Pfizer | Galderma | Janssen | |
| 2 | Consultancy | Galderma | | | |
| 3 | Employment | | | | |
| 4 | Expert testimony | CLL pharma | | | |
| 5 | Grants/grants pending | Candela/synero n | Psoriamed | | |
| 6 | Payment for lectures including service on speakers bureaus | Pfizer | Janssen | MSD | Abbott, Sinclair, La Roche Posay, Almirall, Bioderma, LEO pharma, Merck |
| 7 | Payment for manuscript preparation | | | | |
| 8 | Patents (planned, pending or issued) | | | | |
| 9 | Royalties | | | | |
| 10 | Payment for development of educational presentations | Pfizer | | | |
| 11 | Stock/stock options | | | | |
| 12 | Travel/accommodati ons/meeting expenses unrelated to activities listed** | Pfizer | Janssen | MSD | Abbott, Bioderma |

| | | | | | |
|---|---|---|---|---|---|
| 13 | Other (err on the side of full disclosure) | | | | |

* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | None | | | |

Conflicts of interests: Adrian Tanew, M.D.

| The Work Under Consideration for Publication | | | | | |
|---|---|---|---|---|---|
| | | **Name** | **Name** | **Name** | **Name** |
| 1 | Grant | none | | | |
| 2 | Consulting fee or honorarium | none | | | |
| 3 | Support for travel to meetings for the study or other purposes | none | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | none | | | |
| 5 | Payment for writing or reviewing the manuscript | none | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | none | | | |
| 7 | Other | none | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | none | | | |
| 2 | Consultancy | none | | | |
| 3 | Employment | none | | | |
| 4 | Expert testimony | none | | | |
| 5 | Grants/grants pending | none | | | |
| 6 | Payment for lectures including service on speakers bureaus | none | | | |
| 7 | Payment for manuscript preparation | none | | | |
| 8 | Patents (planned, pending or issued) | none | | | |
| 9 | Royalties | none | | | |
| 10 | Payment for development of educational presentations | none | | | |
| 11 | Stock/stock options | none | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | none | | | |
| 13 | Other (err on the side of full disclosure) | none | | | |

* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | none | | | |

Adrian Tanew, M.D.

Dept Dermatology, Medical University of Vienna, Austria
Vienna, October 17, 2011

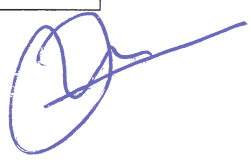
Ao. Univ. Professor
DR. ADRIAN TANEW
Univ. Klinik für Dermatologie
Währinger Gürtel 18-20
A-1090 Wien, Austria
Tel.: +43 1 40 400-7702
Fax: +43 1 408 12 87

## Conflicts of interests

| The Work Under Consideration for Publication | | | | | |
|---|---|---|---|---|---|
| W. van der Veen | | **Name** | **Name** | **Name** | **Name** |
| 1 | Grant | no | | | |
| 2 | Consulting fee or honorarium | no | | | |
| 3 | Support for travel to meetings for the study or other purposes | no | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | no | | | |
| 5 | Payment for writing or reviewing the manuscript | no | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | no | | | |
| 7 | Other | | | | |

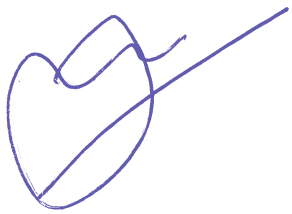
* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | no | | | |
| 2 | Consultancy | no | | | |
| 3 | Employment | no | | | |
| 4 | Expert testimony | no | | | |
| 5 | Grants/grants pending | no | | | |
| 6 | Payment for lectures including service on speakers bureaus | no | | | |
| 7 | Payment for manuscript preparation | no | | | |
| 8 | Patents (planned, pending or issued) | no | | | |
| 9 | Royalties | no | | | |
| 10 | Payment for development of educational presentations | no | | | |
| 11 | Stock/stock options | no | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | no | | | |
| 13 | Other (err on the side of full disclosure) | no | | | |



* This means money that your institution received for your efforts.
** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | no | | | |



J.P.W(ietze) van der veen, M.D., Ph.D.

Netherlands Institute for Pigment Disorders/Department of Dermatology
AMC/University of Amsterdam

17 oct 2011

## Conflicts of interests

| The Work Under Consideration for Publication | | | | | |
|---|---|---|---|---|---|
| N. van Geel | | **Name** | **Name** | **Name** | **Name** |
| 1 | Grant | No | | | |
| 2 | Consulting fee or honorarium | No | | | |
| 3 | Support for travel to meetings for the study or other purposes | No | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | No | | | |
| 5 | Payment for writing or reviewing the manuscript | No | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | No | | | |
| 7 | Other | | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | NO | | | |
| 2 | Consultancy | | | | |
| 3 | Employment | | | | |
| 4 | Expert testimony | | | | |
| 5 | Grants/grants pending | | | | |
| 6 | Payment for lectures including service on speakers bureaus | | | | |
| 7 | Payment for manuscript preparation | | | | |
| 8 | Patents (planned, pending or issued) | | | | |
| 9 | Royalties | | | | |
| 10 | Payment for development of educational presentations | | | | |
| 11 | Stock/stock options | | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | | | | |
| 13 | Other (err on the side of full disclosure) | | | | |

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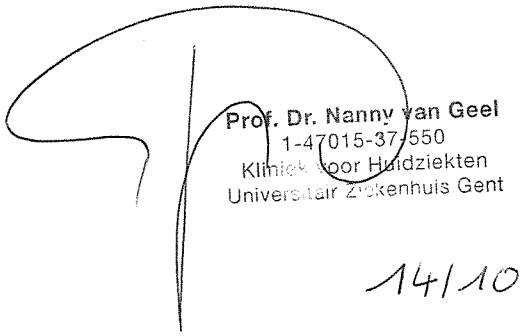
| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | No | | | |




Nanja van Geel

14/10/2011

## Conflicts of interests

| The Work Under Consideration for Publication **EDF-Guidelines for Vitiligo** | | | | | |
|---|---|---|---|---|---|
| | | **Maxine Whitton** | **Name** | **Name** | **Name** |
| 1 | Grant | NO | | | |
| 2 | Consulting fee or honorarium | NO | | | |
| 3 | Support for travel to meetings for the study or other purposes | NO | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | NO | | | |
| 5 | Payment for writing or reviewing the manuscript | NO | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | NO | | | |
| 7 | Other | NO | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | NO | | | |
| 2 | Consultancy | NO | | | |
| 3 | Employment | NO | | | |
| 4 | Expert testimony | NO | | | |
| 5 | Grants/grants pending | NO | | | |
| 6 | Payment for lectures including service on speakers bureaus | NO | | | |
| 7 | Payment for manuscript preparation | NO | | | |
| 8 | Patents (planned, pending or issued) | NO | | | |
| 9 | Royalties | NO | | | |
| 10 | Payment for development of educational presentations | NO | | | |
| 11 | Stock/stock options | NO | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | NO | | | |
| 13 | Other (err on the side of full | NO | | | |

| | | | | | |
|---|---|---|---|---|---|
| | disclosure) | | | | |

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| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | NO | | | |

## Conflicts of interests

| The Work Under Consideration for Publication | | | | | |
|---|---|---|---|---|---|
| | | **Wolkerstorfer Albert** | **Name** | **Name** | **Name** |
| 1 | Grant | None | | | |
| 2 | Consulting fee or honorarium | None | | | |
| 3 | Support for travel to meetings for the study or other purposes | None | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | None | | | |
| 5 | Payment for writing or reviewing the manuscript | None | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | None | | | |
| 7 | Other | None | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | None | | | |
| 2 | Consultancy | None | | | |
| 3 | Employment | None | | | |
| 4 | Expert testimony | None | | | |
| 5 | Grants/grants pending | None | | | |
| 6 | Payment for lectures including service on speakers bureaus | None | | | |
| 7 | Payment for manuscript preparation | None | | | |
| 8 | Patents (planned, pending or issued) | None | | | |
| 9 | Royalties | None | | | |
| 10 | Payment for development of educational presentations | None | | | |
| 11 | Stock/stock options | None | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | None | | | |
| 13 | Other (err on the side of full | None | | | |

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|---|---|---|---|---|---|
| | disclosure) | | | | |

* This means money that your institution received for your efforts.

** For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

| Other relationships | | | | | |
|---|---|---|---|---|---|
| 1 | Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work? | None | | | |

A. Walkers Forter

23-12-2014

## Conflicts of interests

| The Work Under Consideration for Publication | | | | | |
|---|---|---|---|---|---|
| | | **Mauro Picardo** | **Name** | **Name** | **Name** |
| 1 | Grant | | | | |
| 2 | Consulting fee or honorarium | | | | |
| 3 | Support for travel to meetings for the study or other purposes | | | | |
| 4 | Fees for participation in review activities, such as data monitoring boards, statistical analysis, end point committees, and the like | | | | |
| 5 | Payment for writing or reviewing the manuscript | | | | |
| 6 | Provision of writing assistance, medicines, equipment, or administrative support | | | | |
| 7 | Other | | | | |

* This means money that your institution received for your efforts on this study.

| Relevant financial activities outside the submitted work | | | | | |
|---|---|---|---|---|---|
| 1 | Board membership | | | | |
| 2 | Consultancy | | | | |
| 3 | Employment | | | | |
| 4 | Expert testimony | | | | |
| 5 | Grants/grants pending | Giuliani SpA<br>Rottapharm SpA<br>Intendis GmbH | | | |
| 6 | Payment for lectures including service on speakers bureaus | | | | |
| 7 | Payment for manuscript preparation | | | | |
| 8 | Patents (planned, pending or issued) | | | | |
| 9 | Royalties | | | | |
| 10 | Payment for development of educational presentations | | | | |
| 11 | Stock/stock options | | | | |
| 12 | Travel/accommodations/meeting expenses unrelated to activities listed** | Giuliani SpA<br>Ibsa Farmaceutici Italia SpA | | | |
| 13 | Other (err on the | | | | |

| | | | | | |
|---|---|---|---|---|---|
| | side of full disclosure) | | | | |

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| Other relationships | | | | | |
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