

PRESCRIBING INFORMATION

OXSORALEN 10 mg Capsules

(Methoxsalen, USP)

Melanin Repigmentation
Photochemotherapy of Psoriasis and Atopic Dermatitis

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INDICATIONS

Repigmentation of vitiliginous lesions, to protect against solar sensitivity and to promote tanning in persons with very complexion. Oral route is preferred if extensive repigmentation is desired since topical application can only be applied to a small area at a time.

For treatment of psoriasis and atopic dermatitis in combination with high intensity UVA light.

CONTRAINDICATIONS

Hepatic insufficiency. Diseases associated with photosensitivity, such as porphyria, acute lupus erythematosus or infectious leukoderma. Safety in those 12 years and under, in aphasic people, in pregnant women or in women of childbearing age has not been established. In albinism it increases tolerance to sunlight, but has no effect on pigmentation. No preparation with any photosensitizing capacity, internal or external, should be used concomitantly with methoxsalen therapy.

WARNINGS

Methoxsalen is a potent drug and it is recommended that the entire brochure be read before prescribing or dispensing the information. Safety during pregnancy or lactation has not been demonstrated. Use in these conditions should be undertaken only when in the judgment of the physician, the probable benefits outweigh the possible risks.

All patients should wear goggles and should close their eyes during treatment with UV light.

PRECAUTIONS

Should be used only by healthy adults, and use solely to produce a cosmetic tan is not recommended because of its potential toxicity and uncertain results. When used to increase tolerance to sunlight (albinism) and accelerate suntan (people with very light complexion), it should not be given for periods exceeding 2 weeks. When used in patients with vitiligo, liver function tests should be performed monthly for the first few months and occasionally thereafter. If impairment of liver function is suspected, give smaller doses or discontinue drug.

There have not been any clinical reports or tests to verify that more severe reactions may result from the concomitant ingestion of furocoumarin containing food while on methoxsalen therapy; but the physician should warn the patient that taking limes, figs, parsley, parsnips, mustard, carrots, and celery, might increase reactions to sun and artificial light exposure. Methoxsalen should be used with caution in patients with defective coagulation or in those patients being treated with anticoagulant drugs.

ADVERSE EFFECTS

Occasionally nervousness, insomnia or depression may occur. When taken on an empty stomach, nausea may occur. Therefore, it is recommended to take Oxsoralen capsules after meals, or total dosage may be taken in two divided dosages one half an hour apart.

OVERDOSAGE

The dosage of OxSORALEN capsules must be carefully controlled. Overdosage and/or overexposure of light may result in serious burning and blistering. To prevent harmful effects, the physician should carefully instruct the patient to adhere to the prescribed dosage schedule and procedure. If an overdose has been taken, emesis should be encouraged. The treatment for severe reactions resulting from overdosage or overexposure should follow accepted procedures for treatment of severe burn. If overdosage occurred without light exposure, patients should be kept in dark room and avoid total light exposure for at least 24 hours.

DOSAGE AND ADMINISTRATION

OxSORALEN capsules (methoxsalen) should be taken after meals or with milk, or in two divided doses approximately 30 minutes apart, to minimize adverse gastrointestinal effects.

Methoxsalen therapy must be accompanied by some form of UVA irradiation. Initial UV light exposure times should be based on the minimum phototoxic dose (MPD) for the specific light source being used. MPD can be determined by irradiating several skin areas on the patient's back, 2 cm in diameter with varying light exposure times and determining the exposure time that produces erythema at 72 hours. To prevent serious burns following administration of methoxsalen, patients should be carefully instructed not to exceed the recommended dosage and UV light exposure time.

VITILIGO

To repigment vitiliginous areas in adults and children older than 12 years of age, the oral dosage of OxSORALEN (methoxsalen) is 20 mg daily, given as a single dose on a full stomach 3 to 4 hours before measured periods of sunlight or UVA exposure (see Sun Exposure Guide). Therapy should be on alternate days and never on 2 consecutive days. Oral dosages greater than

0.6 mg/kg should not be used, since severe burns may result. Repigmentation of vitiliginous lesions may begin after a few weeks of treatment, but substantial changes usually require 6-9 months of therapy. If follicular repigmentation is not apparent after 3 months of treatment, Oxsoalolen therapy should be discontinued.

For solar sensitivity and tanning (albinism and light complexion): take 20 mg on a full stomach 2 hours before measured periods of exposure to sunlight or ultraviolet irradiation. The exposure time during the first 3 or 4 days should be limited to 30 minutes or less. The exposure time, but not the dosage may be increased thereafter. Therapy is not to be continued for longer than 14 days.

For vitiligo adults and children over 12 years of age take 20 mg 2 to 4 hours before exposure to a source of ultraviolet light. Children 6 to 12 years of age take 10 to 20 mg 2 to 4 hours before light exposure and children up to 6 years of age take 10 mg 2 to 4 hours before light exposure.

Suggested Sun Exposure Guide

(for the treatment of vitiligo and to increase tolerance to sunlight)

The exposure time to sunlight should be limited according to the following schedule:

Basic Skin Colour

Exposure	Light	Medium	Dark
Initial Exposure	15 min	20 min	25 min
Second Exposure	20 min	25 min	30 min
Third Exposure	25 min	30 min	35 min
Fourth Exposure	30 min	35 min	40 min

Subsequent Exposure: gradually increase exposure based on erythema and tenderness.

For photochemotherapy treatment of psoriasis and atopic dermatitis, the appropriate oral dose of Oxisoralen (methoxsalen) is administered on a full stomach 2 to 4 hours before exposure to high-intensity UVA radiation (320-400 nm). Treatments may be administered 2 or 3 times weekly but at least 48 hours apart. The initial dose of Oxisoralen capsules is based on the patient's weight (see Table 1) according to the following schedule:

Table 1:

Weight (kg)	Dose (mg)
< 30	10
30-50	20
51-65	30
66-80	40
81-90	50
91-115	60
> 115	70

The number of methoxsalen doses per week is determined by the patient's schedule of UVA exposures (Table 2). PUVA therapy should not be administered more frequently than once every other day, since the full extent of phototoxic reactions to therapy may not be evident until 48 hours after each exposure. Subsequent treatment with UVA after the initial exposure and provided the patient exhibits no greater than 1 (Table 3) on the erythema scale (minimal perceptible erythema, faint pink), the following schedule of light treatments is recommended (Tables 4 & 5). Before each exposure, the patient is examined for degree of erythema (Table 3). If areas are observed to have greater than grade 1 erythema, treatment should not be continued until the situation is resolved.

Table 2: Initial UVA Exposure Schedule for Oxisoralen

(2 to 4 hours after ingestion of Oxisoralen (methoxsalen) capsules)

Skin Type	History	Exposure Dose (Joules/cm ²) for 2-3 treatments/week		
		Initial	Incremental	Final
I	always burn, never tan	1.5	0.5	0.5
II	always burn, sometimes tan	2.5	0.5	8.0
III	sometimes burn, always tan	3.5	0.5-1.0	12.0
IV	never burn, always tan	4.5	1.0	14.0
V	moderately pigmented individuals; American Indians, Asiatics, Mexicans, Puerto Ricans and Orientals	5.5	1.0	16.0
VI	Black	6.5	1.0-1.5	20.0

Note: Joules/cm² is the radiant energy delivered per square centimeter of skin surface in a given exposure time

- Initial = initial treatment
- Incremental = incremental increase of exposure
- Final = total J/cm² per week

Table 3: Erythema Scale

Grade	Erythema
0	no erythema
1	minimally perceptible erythema - faint pink
2	marked erythema but no edema
3	fiery erythema with edema
4	fiery erythema with edema and blistering

The exposure time can be calculated following the formula below:

$$\text{Time (minutes)} = \frac{16.67 \times (\text{prescribed UVA dose in J/cm}^2)}{\text{Energy output of UVA delivery system in milliwatts/cm}^2}$$

Example: If your measured output is 10 milliwatts/cm² and you wish to deliver a dose of 5 joules, exposure time would be $16.67 \times 5/10 = 8.3$ minutes or 8 minutes 18 seconds.

Table 4: Schedule of Light Treatments for Psoriasis

For Skin Type	Frequency
I, II, III, IV	2 or 3 times/week
V, VI	3 times/week

If the weight of the patient changes during therapy such that the patient would be in a different weight range/dose category, a dose change is usually not necessary; however, if the change in weight is considered sufficiently great, adjustment of methoxsalen dosage and exposure to UVA light should be made accordingly (Table 1). If there is no response or only minimal response after 15 PUVA treatments, the dose of methoxsalen may be increased by 10 mg (a one-time increase); the increased dose may be continued for the remainder of the course of treatment but should not be exceeded. Patients should be clear of psoriasis by the 30th treatment. Patients who are not clear by this time should only be subjected to further treatment after reevaluation by the physician. Maintenance therapy will probably be required to maintain the patient clear of psoriasis. The frequency of maintenance therapy will vary from patient to patient and should be determined on an individual basis.

Extra UVA Exposure to the Lower Legs

Psoriasis present on the lower legs is slow to clear. After the 6th treatment, if psoriasis is present there, the lower legs may receive "extra" UVA. Initially, 0.5 to 1.0 J/cm², depending on the skin type, should be given but as tanning occurs, this may be gradually increased to a maximum of 1/3 of the whole body-UVA dose. The "extra" UVA may be given either before or after the total body treatment, with the rest of the body carefully shielded in order to avoid

overexposure.

Atopic Dermatitis

As for the treatment of psoriasis, the dosage of Oxisoralen (methoxsalen) is based upon the patient's body weight. To obtain acceptable therapeutic results in the treatment of atopic dermatitis, it is necessary to activate the Oxisoralen 2 to 4 hours after ingestion with high intensity UVA light 320-400 nm with peak emission of 340-365 nm. Maintenance treatment will probably be required to maintain the patient clear of atopic dermatitis. The frequency of maintenance therapy will vary from patient to patient and should be determined on an individual basis. Duration of therapy and the maintenance therapy have to be decided on the condition of the patient and the response to PUVA therapy.

Maintenance Therapy

After patients are cleared, they may be assigned a maintenance schedule of treatment once-a-week, once-every-two-weeks, or once-every-three-weeks. The UVA exposure time for the maintenance treatment is the same as the patient's last treatment of the clearing phase and is not changed during maintenance therapy unless the patient develops erythema, psoriasis or atopic dermatitis.

Erythema: during maintenance therapy, the patient's tan and threshold for erythema may gradually decrease. If maintenance treatments produce erythema, the exposure to UVA should be decreased by 0.5 to 1.0 J/cm² per treatment until treatments no longer produce erythema.

Psoriasis and Atopic Dermatitis: If the patient develops new areas of psoriasis or atopic dermatitis during maintenance therapy, the exposure to UVA is increased by 0.5 J/cm² per treatment for patients with a Grade 1 to 2 tanning response (Table 5); by 1.0 J/cm² per treatment for patients with a Grade 3 to 4 tanning response; and by 1.0 to 2.0 J/cm² per treatment for patients with skin types V and VI. This is continued until the psoriasis or atopic dermatitis is

brought under control and the patient is again clear.

Table 5: Tanning Response

- 0 = no change in pigmentation
- 1 = minimally perceptible tan, light brown
- 2 = moderate tan, medium brown pigmentation
- 3 = dark brown pigmentation
- 4 = black pigmentation

Concomitant Therapy

Emollient creams and bath oils: these are to be used regularly during therapy. They will help to remove scales and also prevent excessive dryness.

Topical steroids, tar preparations, salicylic acid and other keratolytics: these preparations may be used on the scalp but are not to be used on the body, except in areas shielded from UVA exposure (e.g., intergluteal folds, soles of feet when upright unit is used, etc.). After exposure to measured periods of sunlight or UVA listed in the above schedule, the skin should be protected from further exposure by applying sunscreens or sun blocking agents. Sunglasses should be worn during exposure and the lips protected with a light-screening lipstick.

AVAILABILITY

Each light pink capsule, printed ICN 600 contains methoxsalen, USP 10 mg. Bottles of 28 and 100 capsules.

PHARMACEUTICAL INFORMATION

Drug Substance: Methoxsalen, USP

Chemical Name: (1) 7*H*-Furo[3,2-*g*][1]benzopyran-7-one,
9-methoxy-;
(2) 9-Methoxy-7*H*-furo[3,2-*g*][1]benzo-
pyran-7-one

Structural Formula:

Molecular Formula: $C_{12}H_8O_4$

Molecular Weight: 216.19

Description: methoxsalen occurs as white to cream-
colored, fluffy, odourless needles
insoluble in water, soluble in acetone

and chloroform

Stability: Oxsolalen capsules should be stored in
well-closed, light-resistant containers at
controlled room temperature (15-30 °C)