

MELADININE

Methoxsalen

In the context of photochemotherapy: psoriasis, vitiligo, mycosis fungoides, cutaneous T cell lymphoma, lichen planus, alopecia totalis, photodermatitis, cutaneous mastocytosis, atopic dermatitis.

FORMS and PRESENTATIONS

Tablet (white): Tube of 30.

Solution at 0.1 % (weak) and 0.75 % (strong) for topical application: Bottles of 24 ml

COMPOSITION

Tablet: per tablet

Methoxsalen 10 mg

Excipients: corn starch, lactose, talc, saccharose, gum arabic, magnesium stearate.

0.1% Solution (weak): per bottle

Methoxsalen 24 mg

Excipients: macrogol 300, glycerol, alcohol.

0.75% Solution (strong): per bottle

Methoxsalen 180 mg

Excipients: acetone, propylene glycol, alcohol.

INDICATIONS

In the context of photochemotherapy: psoriasis, vitiligo, mycosis fungoides, cutaneous T cell lymphoma, lichen planus, alopecia totalis, photodermatitis, cutaneous mastocytosis, atopic dermatitis.

DOSAGE AND ADMINISTRATION

Tablet:

Patient:

up to 30 kg: 1 tablet / treatment;

31 to 50 kg: 2 tablets / treatment;

51 to 65 kg: 3 tablets / treatment;

66 to 80 kg: 4 tablets / treatment;

81 to 90 kg: 5 tablets / treatment;

over 90 kg: 6 tablets/ treatment.

Administration of Meladinine must be followed 2 or 3 hours later by exposure to the sun or to a source of UVA irradiation.

- Exposure to the sun

(often recommended in the treatment of vitiligo): this must be gradual, 10 to 15 minutes at the start of therapy.

Exposure time may be extended to 30 minutes or even 1 hour if the erythema caused by the treatment is not excessive.

Note: erythematous reactions are observed 48 hours after exposure. The exposure time can therefore only be increased with a minimum of risk every other day.

- UVA irradiation (photochemotherapy, PUVA therapy):

this requires special equipment with lamps emitting a UVA spectral output between 320 and 380 nm, with a peak at 365 nm, and emitting almost no UVB irradiation.

The treatment modalities (duration, frequency) depend on lamp intensity and the patient's phototype.

Phototypes UVA doses (Joule/cm²)

initial traitement progression

Always burns, never tans 0.5 0.5

Always burns, tans minimally 1 0.5

Sometimes burns, always tans 1.5 0.5/1

Never burns, always tans 2 1

Dark skin

(Asians, North Africans) 3.5 1/1.5

Blacks

The exposure time can also be determined by the minimal phototoxic dose (MPD).

The treatment schedule is 2 to 4 times a week, according to the indication.

The exposure time determined according to phototype or MPD is increased at each treatment, depending on the patient's tolerance and response.

Do not exceed the maximum UVA dose per treatment, which ranges from 10 Joule/cm² for type I to 20 Joule/cm² for type VI.

Usually, 15 to 25 treatments are necessary to obtain satisfactory clearance of psoriasis.

Mucosis fungoides requires more treatments.

Maintenance therapy (from once a week to once a month) is carried out with the same dose as that used at the last treatment.

Modalities may differ for patients who respond poorly to the conventional treatment.

This can be adjusted for individual kinetics.

Daily treatment cost: €0.11 to €0.67.

Solution for topical application:

Meladinine 0.75% strong solution should be used only rarely and only after first using the 0.1% weak solution.

Treatment with topical applications of Meladinine solution should be restricted to small, localized lesions easy to protect from sun overexposure. Always begin by using the 0.1% weak solution (which may be further diluted with 60° alcohol to lower the concentration two- or four-fold, if necessary). Treatment should be conducted with extreme caution so as to avoid any risk of burning. Apply the solution with a cotton swab, taking care to keep away from the lesion periphery

so as to avoid causing unsightly peripheral hyperpigmentation.

- Irradiation by exposure to the sun:

This is done in late afternoon. Considering that erythema does not occur until 48 hours after exposure, at the start of therapy allow an interval of 48 hours between treatments.

Exposure times should not be exceeded and should be increased very gradually:

1st week: 1/4 minute,

2nd week: 1/2 minute,

3rd week: 1 minute,

4th week: 1.5 to 2 minutes.

Exposure time should only be increased if the erythema 48 hours after the last treatment was not too severe.

In case of excellent tolerance (very dark skin), the strong solution may be used after 3 or 4 weeks by returning to a ¼ minute exposure time. The exposure time is then increased gradually.

- Irradiation by UVA (PUVA therapy):

Exposure to UVA lamps, 1 hour after applying the solution, should be gradually increased from a starting dose of 0.25 to 0.50 Joule/cm² at the first treatment. Exposure should be increased by increments of 0.25 Joule/cm² from one treatment to the next. In case of severe erythema or pruritus, the treatment should be discontinued momentarily, then resumed at a dose that does not exceed half of the previous dose.

DOSAGE AND ADMINISTRATION (continued)

- Balneo-PUVA therapy:

This combines a methoxsalen bath and UVA irradiation. The bath is prepared by diluting a bottle of Meladinine 0.75% strong solution in 80 to 100 liters of water, to obtain a methoxsalen concentration of 1.8 to 2.2 mg per liter (equivalent to 2 bottles for a 150-160 liter adult-size bathtub).

The bath lasts for 15 minutes and is followed by irradiation immediately after drying (patting dry without rubbing).

The recommended UVA doses are lower. The dose for the first treatment is 0.20 Joule/cm², and is gradually increased by 0.02 to 0.05 Joule/cm² at each treatment to a maximum of approximately 1 Joule/cm².

At the end of each irradiation treatment (sun or UVA):

The treated areas should be thoroughly rinsed and protected from any overexposure to the sun by wearing appropriate clothing, gloves, scarf, etc. For uncovered areas that cannot be protected, a total sunscreen should be applied for at least 24 hours following each treatment.

CONTRAINDICATIONS

Due to Meladinine:

Tablet:

Heart failure.

Hepatic and renal insufficiency.

Hypertension.

Tablet and solutions for topical application:

Use for cosmetic purposes, for tanning.

Skin conditions worsened by the sun (lupus erythematosus, porphyria).

Due to PUVA therapy:

Cataract.

History of skin cancer.

Previous arsenic therapy, ionizing radiation.

Children.

WARNINGS and PRECAUTIONS FOR USE

Warnings:

Meladinine must not be used for cosmetic purposes, in particular for tanning: risk of burning.

Precautions for use:

Any exposure to the sun following oral administration or topical application of Meladinine leads to a high risk of burning. Strictly follow the gradual increase in UV exposure times (sun or lamp) and, after each treatment, avoid any additional exposure to the sun by keeping covered and, for exposed areas, by using a total sunscreen, so as to avoid a risk of burning (these precautions must be even more strictly followed in case of local treatment).

Advise patients to wear UVA-absorbing black sunglasses during treatments and for the next 8 to 10 or even 24 hours.

In young women, recommend the use of contraception throughout the duration of therapy.

Take into account the potential long-term risks of photochemotherapy, for which the patient must be closely monitored: skin aging, pigmentary changes, risk of inducing squamous cell carcinoma, risk of cataract formation.

INTERACTIONS

Avoid the concomitant use of other photosensitizing agents.

PREGNANCY and LACTATION

Animal studies indicate that methoxsalen is not teratogenic.

In humans, clinical data on a small number of exposed pregnancies do not indicate any specific malformation. However, the lack of data justifies avoiding the use of this treatment during pregnancy.

UNDESIRABLE EFFECTS

Tablet and solutions for topical application:

Cases of severe burning have been reported.

Effects related to UVA overdose: pruritus, post-PUVA erythema, photo-allergic reactions, Koebner phenomenon, induction of bullous pemphigoid, lupus erythematosus.

Tablet:

Effects specific to methoxsalen: gastric pain, abdominal discomfort, nausea (which can be attenuated by taking the tablets with food, milk in particular).

PHARMACODYNAMICS

Photosensitizing agent (D: dermatology).

Methoxsalen (or 8-methoxypsoralen) has photodynamizing capacity which sensitizes the skin to the action of solar or artificial ultraviolet radiation.

Its spectrum of action is between 320 and 380 nm, with peak efficacy at 365 nm.

PHARMACOKINETICS

Oral administration of methoxsalen induces cutaneous photosensitization which reaches a peak between 2 and 4 hours and disappears after 6 to 8 hours.

90% of the product is excreted in the urine in 12 hours, as hydroxylated derivatives or glucurono-conjugates.

Wide individual variations are seen.

PRESCRIPTION/SUPPLY/REIMBURSEMENT

LIST I

Marketing Authorization No. 306 566.1 (1953/95) tablet

306 567.8 (1953/95) weak solution.

306 568.4 (1953/95) strong solution.

Price: €3.33 (30 tablets).

€2.87 (weak solution).

€3.37 (strong solution).

65% reimbursement by national health insurance. Healthcare establishments.

Marketing Authorization Holder: CLS Pharma contact@clspharma.fr