



## TECHNICAL DATA SHEET

1293-TDS-ENG-2023

<b>METOXSALENO (8-metoxipsoraleno) (USP)</b>		
DESCRIPTION DCI: METHOXSALEN		DESCRIPTION DOE: METOXALENO
CAS N°: 298-81-7	EC N°: 206-066-9	AEMPS CODE: 1962A
MOL. WEIGHT: 216.19	MOL. FORMULA: C <sub>12</sub> H <sub>8</sub> O <sub>4</sub>	ARTICLE CODE: 1293

ATTRIBUTES	SHOULD BE
Appearance	White crystalline powder
Identification A	Complies
Identification B	Complies
Assay	98.0 - 102.0 %
Residue on ignition	=< 0.1 %
Organic impurities	
Related compound A	=< 0.15 %
Related compound B	=< 0.15 %
Unspecified impurities	=< 0.10 %
Total impurities	=< 0.5 %
Water	=< 0.5 %

### COMPLIES WITH

USP 2023

### STORAGE

Store in a tightly closed containers, in a dry and well-ventilated place.

### REMARKS

Methoxsalen is subjected to the requirements of the ICH Q3D "Elemental Impurities" guideline and the requirements of guides EMA/CHMP/ICH/82260/2006.

Absence of N-nitrosamines impurities has been ensured after a risk evaluation according to ICH Q9, ICH M7 and in accordance with guidelines EMA/428592/2019 Rev 2 and EMA/189634/2019.

Certificates of residual solvents, allergens, non-GMO and BSE-TSE, among others, are available upon request.

All methods of analysis are validated by official pharmacopoeias or are validated by internal methods of the manufacturer, which can be obtained at specific request. The above information does not exempt from the obligation to identify the product before use.

### Properties and uses

METHOXSALEN is a component of the fruits of the Ammi majus (family Umbelliferae).

It has good oral absorption, and binds strongly to plasma proteins. It usually accumulates in the epidermal cells, and diffuses to the eye lenses. It is completely metabolized, and approximately 95% of the dose is excreted in the urine in the first 24 h.

It is a powerful photosensitizer of the skin, especially with long wave UV light (320 - 400 nm). Photosensitization selectively inhibits the epidermal synthesis of DNA without inhibition provided by the production of epidermal cells. The improvement in cell damage can be followed by melanization and pigmentation of the epidermis by the melanocytes.

After ingestion, it appears at 1-4 h after administration, and disappears after about 8 h. Topical application is more effective and the highest sensitivity persists for several days.

Exposure of patients treated with METHOXSALEN to UV light thickens the stratum corneum. It produces an inflammatory reaction of the skin and increases the concentration of melanin in the exposed area.

It is used in conjunction with UVA light to treat idiopathic vitiligo (unless accompanied by destruction of melanocytes, which



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would be ineffective) and severe or generalized psoriasis that does not respond to topical therapy.

It is also used in mycosis fungoides, T-cell lymphomas, and under rigorous medical control to increase the tolerance of skin hypersensitive to sunlight.

It is incorporated to the O / W emulsions at the end, cold, making a paste with propylene glycol, glycerin, or sorbitol, or with liquid petrolatum if it is W / O.

### Dosage

For vitiligo

Oral route, 20 mg taken 2-4 h before controlled exposure to sunlight or UVA, 2-3 times per week. Never exceed 0.6 mg / Kg  
Topical route, 0.01 - 1% in fluid solutions or O / W nonionic emulsions, in case the area to be treated is less than 20%, immediately before receiving the phototherapy or until 2.5 h before (according to the physician), a or more times a week.

For psoriasis

Oral route: 10 - 70 mg according to weight, taken 2 h before receiving phototherapy, 2 or more times a week. Never exceed 0.6 mg / Kg.

Topical route: at 0.015 - 0.15%, applied 15 minutes before receiving phototherapy.

### Side effects

Gastrointestinal discomfort may occur after oral administration, and CNS toxicity may be less frequent.

In prolonged therapies it can produce premature wrinkles, premature aging of the skin, precancerous lesions, phototoxicity, dermal pain, hypertrochosis, depigmentation of the skin, and increased likelihood of skin cancer.

After sun exposure serious burns may appear. Increases the likelihood of cataracts.

### Contraindications

It is contraindicated in hepatic insufficiency and in diseases accompanied by photosensitivity such as porphyria, acute lupus erythematosus, and polymorphic eruptions by light.

It is also contraindicated in allergies to psoralens, aphakia (absence of a crystalline lens), and in skin cancer or a history of skin cancer. Therapy with psoralens and UVA in children is not recommended.

### Precautions

It should not be administered simultaneously with any medication or other products for external or internal use that cause photosensitization.

Do not take foods that increase the sensitivity of the skin to sunlight (eg carrots, celery, parsnips, parsley ...).

Do not sunbathe between 24 h before and 48 h after receiving UV phototherapy. Avoid sun exposure (even through crystals or cloudy weather) at least 8 h after the intake of METHOXSALEN, you must wear clothes and wear glasses that absorb UVA light 24 hours after ingestion.

The photosensitivity is longer after topical application, and the treated skin should be protected from sunlight for at least 12-48 h. Protect the skin throughout the day with sunscreens, lips, and eyes.

It is necessary to protect the skin of the male genitals during treatment.

Ophthalmological controls, antinuclear antibody titers, and hepatic functions are recommended, which will be carried out before starting therapy and subsequently at periodic intervals. The signs of remalignity or malignancy of the skin lesions should be studied.

### Interactions

It is a potent inhibitor of caffeine metabolism. Phenytoin decreases its plasma concentration, possibly by induction of liver enzymes.

### Incompatibilities

Alkalis



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### Other observations

It is termolabile and photosensitive. It should be used only under strict medical supervision.

### Formulation examples

#### *METHOXSALEN in emulsion*

METHOXSALEN - **0.25 %**

Emulsion O / W c.s.p. - **60 g**

Modus operandi: Put the METHOXSALEN in a mortar and add a bit of glycerin to form a paste. Gradually add the O / W emulsion.

#### *METHOXSALEN in alcohol solution*

METHOXSALEN - **1 %**

Propylene glycol - **50 mL**

Alcohol 96% - **50 mL**

Modus operandi: Dissolve METHOXSALEN in the solvent mixture.

#### *METHOXSALEN in oil*

METHOXSALEN - **0.1 %**

Olive oil c.s. - **30 mL**

Modus operandi: Interpose the METHOXSALEN in the olive oil, stirring constantly.

#### *METHOXSALEN in capsules*

METHOXSALEN - **50 mg**

for 1 capsule, No. 20.

Modus operandi: No. 4 capsules with enteric coating are used.