PRODUCT MONOGRAPH

DIMETHYL SULFOXIDE IRRIGATION USP
(Dimethyl Sulfoxide)

500mg/g

Intravesical Instillation for the Treatment of Interstitial Cystitis

Sandoz Canada Inc.
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Control # 100328

PRODUCT MONOGRAPH

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DIMETHYL SULFOXIDE IRRIGATION USP

500 mg/g (50% w/w)

Not for IM or IV Injection

THERAPEUTIC CLASSIFICATION

Intravesical Instillation for the Treatment of Interstitial Cystitis

ACTIONS AND CLINICAL PHARMACOLOGY

Dimethyl Sulfoxide has a wide spectrum of primary pharmacological activity, including: membrane penetrant, solute "carrier" across membranes, anti-inflammatory, analgesia, diuresis, cholinesterase inhibitor, muscle relaxation, vasodilator.

The mode of action of Dimethyl Sulfoxide Irrigation USP as a treatment for interstitial cystitis is speculative at this time. Hypothesis center around following:

a) Anti-inflammation
b) Analgesic
c) Improvement of blood supply
d) Softening of collagen due to action on cross-linking.

Dimethyl sulfoxide is metabolized by oxidation to dimethyl sulfone or by the reduction to dimethyl sulfide. Dimethyl sulfoxide and dimethyl sulfone are excreted in the urine and feces. Dimethyl sulfide is eliminated through the breath and skin and is responsible for the characteristic odour from patients on dimethyl sulfoxide medication. Dimethyl sulfone can persist in serum for longer than two weeks after a single intravesical instillation. No residual accumulation of dimethyl sulfoxide has occurred in man or lower animals who have received treatment for protracted periods of time. Following topical application dimethyl sulfoxide is absorbed and generally distributed in the tissues and body fluids.

INDICATIONS AND CLINICAL USE

Dimethyl Sulfoxide Irrigation USP is indicated for the symptomatic relief of patients with interstitial cystitis. Dimethyl Sulfoxide Irrigation USP has not been approved as being safe and effective for any other indication. There is no clinical evidence of effectiveness of dimethyl sulfoxide in the treatment of bacterial infections of the urinary tract.

CONTRAINDICATIONS

None.

WARNINGS

Dimethyl Sulfoxide Irrigation USP can initiate the liberation of histamine and there has been an occasional hypersensitivity reaction with topical administration of dimethyl sulfoxide. This hypersensitivity has not occurred in patients receiving intravesical Dimethyl Sulfoxide Irrigation USP; however, the physician should be cognizant of this possibility in prescribing Dimethyl Sulfoxide Irrigation USP. If anaphylactoid symptoms develop, appropriate therapy should be instituted. Some data indicates that dimethyl sulfoxide potentiates other concomitantly administered medications.

PRECAUTIONS

Changes in the refractive index and lens opacities have been seen in monkeys, dogs and rats given dimethyl sulfoxide chronically. No ophthalmic changes attributable to intravesical instillation of dimethyl sulfoxide have been reported in patients carefully followed for up to 17 months; nevertheless, full eye evaluations, including slit lamp examinations are recommended prior to and at six month intervals during treatment. Along with the ophthalmological examinations, patients should be investigated with respect to biochemical parameters, particularly renal and hepatic function, at six month intervals.

Intravesical instillation of Dimethyl Sulfoxide Irrigation USP may be harmful to patients with urinary tract malignancy because of dimethyl sulfoxide-induced vasodilation.

Use in pregnancy:

The safety of dimethyl sulfoxide for the human fœtus has not been established, hence it should be given to pregnant women only when the potential benefits to the mother have been weighed against possible hazards to the child.

Use in Nursing Mothers:

Mothers receiving dimethyl sulfoxide should not nurse their infants. It must be assumed, although data are lacking, that dimethyl sulfoxide is excreted in human milk.

ADVERSE REACTIONS

A garlic-like taste may be noted by the patient within a few minutes after instillation of Dimethyl Sulfoxide Irrigation USP. This taste may last several hours and because of the presence of metabolites, an odour on the breath and skin may remain for 72 hours. Transient chemical cystitis has been noted following instillation of 100% dimethyl sulfoxide.

The patient may experience moderately severe discomfort on administration. Usually this becomes less prominent with repeated administration.

DOSAGE AND ADMINISTRATION

Instillation of 50 mL of Dimethyl Sulfoxide Irrigation USP directly into the bladder may be accomplished by catheter or aseptic syringe and allowed to remain for 15 minutes. Application of an analgesic lubricant gel such as lidocaine jelly to the urethra is suggested prior to insertion of the catheter to avoid spasm. The medication is expelled by spontaneous voiding. It is recommended that treatment be repeated every two weeks until maximum symptomatic relief is obtained. Thereafter, time intervals between therapy may be increased appropriately. In selected cases where symptomatic relief is not complete, the bladder may be gently distended by gravity instillation with up to 500 mL of a solution prepared immediately prior to instillation in a glass vial, with one part Dimethyl Sulfoxide Irrigation USP and one part sterile water prior to the instillation of the standards dose of 50 mL of Dimethyl Sulfoxide Irrigation USP. After retention of Dimethyl Sulfoxide Irrigation USP for 15 minutes the medication is again expelled by spontaneous voiding. Administration of oral analgesic medication or suppositories containing belladonna and opium prior to instillation of Dimethyl Sulfoxide Irrigation USP can reduce bladder spasm in particularly sensitive patients.

In patients with very sensitive bladders, the initial treatment should be done under anesthesia (preferably saddle block type).

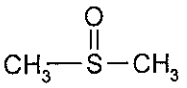
Dimethyl Sulfoxide Irrigation USP is recommended for bladder instillation only.

Remove both the aluminium seal and rubber stopper prior to withdrawing contents of the bottle.

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Dimethyl Sulfoxide
Chemical name:
Structural Formula:



Molecular Formula: C_2H_6OS

Molecular Weight: 78.14

Description: Clear, colourless and essentially odourless liquid which is miscible with water and most organic solvents.

Melting Point: 18.4 °C

Boiling Point: 189 °C

Specific Gravity: 1.100

COMPOSITION

Each mL of sterile and pyrogen free Dimethyl Sulfoxide Irrigation USP contains: Dimethyl Sulfoxide 50% w/w in water for injection.

STORAGE AND STABILITY RECOMMENDATIONS

Single use vials. Discard unused portion.
Store between 15 and 30 °C. Protect from light. Do not autoclave.

AVAILABILITY OF DOSAGE FORMS

Dimethyl Sulfoxide Irrigation USP is available in 50 mL clear glass bottles, boxes of 1.

PHARMACOLOGY

Dimethyl sulfoxide in some lower animals, including rabbits, dogs, and pigs has been shown to produce changes in the refractive index of the lens of the eye. The oral route appears more likely to cause such ocular changes which occur at doses of 1 g/kg/day of dimethyl sulfoxide for treatment periods as short as 69 days. The rabbit was the most susceptible of the species treated while the rhesus monkey was most resistant.

TOXICITY

A refractive index change in the lens (not an opacity) had been observed after 3 months at a dose of approximately 5 g/kg in dogs, rabbits and pigs. No microscopic or chemical differences could be found between the lenses of the treated animals and the controls. In the affected animals, there appeared two distinct zones of different refraction. This could easily be observed with an ophthalmoscope and with a slit lamp. It appeared to be a dose-related effect, and it diminished as the dose was reduced. It is noteworthy that the effect was produced 50 to 100 times the usual human therapeutic dose.

Extensive toxicology studies have been conducted in numerous animal species, at 3 to 30 times the dose anticipated for humans, for periods of up to 18 months. Dimethyl Sulfoxide appears to be a relatively safe drug for human administration and the lens changes which have been noted in animals have not yet been reported in humans.

Dimethyl sulfoxide caused teratogenic responses in hamsters, rats and mice when administered intraperitoneally at high doses (5-12 g/kg). Oral or topical doses of dimethyl sulfoxide did not cause problems of reproduction in rats, mice or hamsters.

Topical doses (5 g/kg – first two days, then 2.5 g/kg – last eight days) produced terata in rabbits, but in another study, topical doses of 1.1 g/kg days three through sixteen of gestation failed to produce any abnormalities.

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