

# DATASHEET

## Myocrisin®

### Name of the Medicine

#### Non-proprietary Name

Sodium aurothiomalate

### Description

Each ampoule of MYOCRISIN solution for injection contains 2% w/v (10mg), 4% w/v (20mg) or 10% w/v (50mg) of sodium aurothiomalate and phenylmercuric nitrate and water for injections.

### Pharmacology

#### Site and Mode of Action

In rheumatoid arthritis, MYOCRISIN appears to suppress the disease processes in two ways. Firstly it penetrates into the joint cavity and affects the lysosomal membranes. Secondly, it binds to plasma proteins, including IgG, the rheumatoid factor and the immune complex so that when the lysosomes ingest immune complex the gold is absorbed with it and inactivates lysosomal enzymes within the cell.

#### Pharmacokinetics

Gold is completely absorbed from an intramuscular injection of MYOCRISIN. It is distributed widely to many tissues including erythrocytes and is highly protein bound, mainly to albumin. The initial plasma half-life is 5.5 days, the terminal half-life is around 250 days. The apparent half-life in synovial fluid is 6-7 days. Gold is subject to significant excretion in the urine and faeces.

### Indications

MYOCRISIN is indicated in the management of active progressive rheumatoid arthritis, and progressive juvenile chronic arthritis, especially if polyarticular or seropositive.

### Contraindications

Hypersensitivity to any component of this product. Patients with gross renal or hepatic disease, diabetes, marked toxæmia, a history of blood dyscrasias or exfoliative dermatitis.

Use in Pregnancy is contraindicated (See Precautions).

### Precautions

Every candidate for gold therapy should be investigated fully to prevent the administration of gold to those with gross renal or hepatic defects, diabetes, marked toxæmia, a history of blood dyscrasias or dermatitis. Before starting treatment, and again before each injection, the urine should be tested for protein, the skin inspected for rashes, and a full blood count performed, with a numerical platelet count (not an estimation). The availability, whenever possible, of the results of blood counts before the next injection is a useful aid in minimising toxic reactions. Minimum values below which gold should not be given until the count has been repeated and there is return to normal values are: total white cells 4,000/mm<sup>3</sup>, neutrophils 2,000/mm<sup>3</sup>, platelets 150,000/mm<sup>3</sup>. It is unwise to continue with gold injections when there is a persistent or otherwise unexplained eosinophilia exceeding 1,000/mm<sup>3</sup>, as this may indicate an impending toxic reaction. Particular vigilance should be maintained during the period when between 300 to 500mg of gold has been given because it is at this time that a blood dyscrasia is most likely to occur.

If the full blood count is normal after the cumulative gold dose reaches 500mg, and provided the full blood count remains normal, full blood counts can be done before every second injection. The presence of proteinuria, pruritus, or rash, or an eosinophilia are indications of developing toxicity; the dose of MYOCRISIN should be withheld for one to two weeks until all signs have disappeared, when the treatment may be restarted on a smaller dosage.

MYOCRISIN may be given in the presence of a trace of protein, but if there is 30mg/100mL or more, in the absence of urinary infection or other cause it may indicate a developing gold nephropathy and the treatment should be stopped.

Generally, this induces a complete reversal although in some instances the proteinuria may persist for many months.

The complaint of metallic taste, sore throat, glossitis, buccal ulceration and or easy bruising or bleeding demands an immediate blood count, followed, if indicated, by appropriate treatment for agranulocytosis and or thrombocytopenia. All patients receiving the drug should be warned both verbally and in writing to report immediately the appearance of sore throat, mouth or tongue, or the development of bruising or unusual bleeding.

As gold preparations cause ocular adverse effects, ophthalmological examination is recommended if ocular symptoms occur.

MYOCRISIN should be used with care in patients with marked hypertension or compromised cerebral or cardiovascular circulation.

As with other gold preparations, reactions which resemble anaphylactoid effects have been reported. These effects may occur after any course of therapy within the first 10 minutes following drug administration (see Dosage and Administration). If anaphylactoid effects are observed, treatment with MYOCRISIN should be discontinued.

MYOCRISIN is unlikely to produce an effect on the ability to drive or use machinery.

### **Use in Pregnancy**

Category B2

Like other heavy metals, gold may pass the placental barrier and may cause foetal damage; therefore, it should not be given during pregnancy, but as rheumatoid arthritis usually shows an improvement at this time, the withdrawal of gold is more than justifiable.

### **Use in Lactation**

The presence of gold has been demonstrated in the milk of lactating mothers and in the serum and red blood cells. The use of MYOCRISIN for nursing mothers is not recommended.

### **Interactions with other Medicines**

Gold salts should not be used concomitantly with penicillamine.

Extra caution should be exercised if phenylbutazone or oxyphenbutazone are administered concurrently.

Gold administration may exacerbate aspirin induced hepatic dysfunction.

Caution is needed in patients treated concomitantly with sodium aurothiomalate and angiotensin-converting enzyme inhibitors due to an increased risk of severe anaphylactoid reactions in these patients.

### **Adverse Effects**

These appear to be associated with individual tolerance, and may be largely avoided by careful titration of dosage. Skin rashes are frequent and commonly benign, but as such reactions may be the forerunners of severe gold toxicity, they must never be treated lightly. Skin complications include pruritus, erythema and transient eczema. Proteinuria is less common and indicates caution, but heavy proteinuria is a sign of more serious nephritis such as nephrotic syndrome or glomerulonephritis.

There have been some reports of gold deposits in the lens or cornea of patients treated with gold. These deposits have not led to any eye disorders or any degree of visual impairment, and have cleared within 3-6 months of cessation of therapy.

Haematuria may also develop. The most severe reactions due to gold are agranulocytosis, thrombocytopenia or aplastic anaemia; these occur usually in sensitive patients when a total of about 300mg has been given.

Stomatitis and oral mucous membrane reactions (such as ulcers) have been observed. Reactions of the "nitroid type" which may resemble anaphylactoid effects have been reported. Flushing, fainting, dizziness and sweating are most frequently reported.

#### **Other Reactions Include:**

Gastrointestinal reactions such as nausea, vomiting, anorexia, abdominal cramps, diarrhoea, ulcerative enterocolitis; reactions involving the eye such as iritis, corneal ulcers, gold deposits in ocular tissues; peripheral neuropathy, elevated spinal fluid protein; CNS complications including confusion, hallucinations and seizures; hepatitis; jaundice; gold bronchitis; pulmonary injury manifested by interstitial pneumonitis and fibrosis; alopecia; fever; arthralgia.

Treatment with MYOCRISIN should be discontinued immediately when toxic reactions occur.

MYOCRISIN should not be reinstated after severe or idiosyncratic reactions.

#### **Dosage and Administration**

MYOCRISIN should be administered only by intramuscular injection.

Because of the possibility of an anaphylactic reaction, it is recommended that patients be kept under medical observation for a period of 30 minutes after administration of the drug.

Do not use a darkened solution (more than pale yellow).

#### Adults

An initial test dose of 10 mg should be given in the first week followed by weekly doses of 50 mg until signs of remission occur. At this point, 50 mg doses should be given at two week intervals until full remission occurs. With full remission, the interval between injections should be increased progressively to three, four and then (after 18 months to 2 years) to six weeks. If after reaching a total dose of 1 gram (excluding the test dose) no major improvement has occurred and the patient has not shown any signs of gold toxicity, six 100 mg injections may be administered at weekly intervals. If no signs of remission occur after this time, other forms of treatment are to be considered.

#### Elderly

No specific recommendations but elderly patients should be monitored with extra caution.

#### Children

##### Progressive juvenile chronic arthritis

Weekly doses of 1 mg/kg should be given but not exceeding a maximum weekly dose of 50 mg. Depending on urgency, this dose may be preceded by a smaller test dose such as 1/10th or 1/5th of the full dose for 2-3 weeks. Continue weekly doses until signs of remission appear, then increase intervals between injections to two weeks. With full remission, increase interval to three then four weeks. In the absence of signs of remission after twenty weeks consider raising the dose slightly or changing to other therapy. Treatment should be continued for six months. Response can be expected when a total dose of the 300-500 mg has been administered. If patients respond, maintenance therapy should be continued with the dosage administered over the previous 2-4 weeks for 1-5 years.

#### **Overdosage**

The appearance of side effects indicates that the individual is receiving more gold than the system can assimilate. Subsequent dose should be withheld or reduced until the reactions have disappeared and the blood count is normal. Skin reactions should be treated with systemic and topical antihistaminics and corticosteroids. If agranulocytosis, thrombocytopenia or aplastic anaemia is diagnosed, immediate injection of dimercaprol, with corticosteroids, androgens and penicillamine orally, must be given. Fresh blood and/or platelet transfusions should be given with reversed barrier nursing pending recovery of the bone marrow.

Contact the Poisons Information Centre for advice on management of overdosage.

**Presentation and Storage Conditions**

MYOCRISIN 10mg/0.5mL, 20mg/0.5mL, 50mg/0.5mL ampoules are available in packs of 10.

Protect from light. Store below 25°C. Solutions which have darkened in colour must not be used.

**Medicine Classification**

Prescription Medicine.

**Further Information**

Some rheumatologists provide their patients with a 'gold card' on which is recorded the amount of gold salt injected and results of laboratory tests, at the same time issuing a pro forma for further treatment to the general practitioner responsible for the management of the patient. These are valuable aids in the early detection, and so reduce the incidence of toxic reactions.

**Name and Address of the Sponsor**

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