# DATA SHEET

## 1 PRODUCT NAME

MYOCRISIN 10 mg solution for injection

MYOCRISIN 20 mg solution for injection

MYOCRISIN 50 mg solution for injection

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Excipient with known effect: phenylmercuric nitrate.

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Solution for injection.

Clean bright, almost colourless solution.

## 4 CLINICAL PARTICULARS

### 4.1 THERAPEUTIC INDICATIONS

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

### 4.2 DOSE AND METHOD OF ADMINISTRATION

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 (see section 4.4).

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

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.

### Dose

#### *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.

#### *Paediatric population*

*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.

### Method of administration

MYOCRISIN should be administered only by intramuscular injection.

## 4.3 CONTRAINDICATIONS

Hypersensitivity to sodium aurothiomalate or to any of the excipients listed in section 6.1.

Patients with severe renal or hepatic disease, diabetes, marked toxaemia, a history of blood dyscrasias or exfoliative dermatitis, a history of systemic lupus erythematosus.

Use in pregnancy is contraindicated (see section 4.6).

## 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

MYOCRISIN should be administered with extra caution:

- in patients with a history of enterocolitis or pulmonary fibrosis
- in patients with a history of urticaria
- in patients with a history of eczema
- in the elderly

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 toxaemia, 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) and the readings plotted. 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/$mm^3$, neutrophils 2,000/$mm^3$, platelets 150,000/$mm^3$. It is unwise to continue with gold injections when there is a persistent or otherwise unexplained eosinophilia exceeding 1,000/$mm^3$, as this may indicate an impending toxic reaction. Particular vigilance should be maintained during the period when between 300 to 500 mg 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 500 mg, and provided the full blood count remains normal, full blood counts can be done before every second injection. The presence of proteinuria (including albuminuria), 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 (test dose) followed by a decreased frequency of gold injections.

MYOCRISIN may be given in the presence of a trace of protein, but if there is 30 mg/100 mL 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, aplastic anaemia and or thrombocytopenia. All patients receiving the drug should be warned both verbally and in writing to report immediately the appearance of pruritus,

metallic taste, sore throat, mouth or tongue, stomatitis, buccal ulceration or the development of bruising or unusual bleeding, purpura, epistaxis, bleeding gums, menorrhagia or diarrhoea.

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 and anaphylactoid reactions may occur after any course of therapy within the first 10 minutes following drug administration (see section 4.2). If anaphylactoid effects are observed, treatment with MYOCRISIN should be discontinued.

## 4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

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.

## 4.6 FERTILITY, PREGNANCY AND LACTATION

### Pregnancy

Category B2

Female patients receiving MYOCRISIN should be instructed to avoid pregnancy.

Like other heavy metals, gold may pass the placental barrier and may cause foetal damage; therefore, pregnant patients should not be treated with MYOCRISIN (see section 4.3), but as rheumatoid arthritis usually shows an improvement at this time, the withdrawal of gold is more than justifiable.

### Breast-feeding

The presence of gold has been demonstrated in the milk of lactating mothers and in the serum and red blood cells. Lactating mothers should not breast feed their infants.

**Fertility**

No data available.

## 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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

## 4.8 UNDESIRABLE 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 (including albuminuria) 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 300 mg has been given. Blood disorders including pancytopenia, leucopenia, neutropenia and eosinophilia have also been reported.

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

Nervous system disorders that have been reported are: peripheral neuropathy, Guillain-Barré syndrome and encephalopathy.

Hepatotoxicity with cholestatic jaundice is a complication which may occur early in the course of treatment. It subsides on withdrawing MYOCRISIN.

Severe skin reactions including exfoliative dermatitis and dermatitis bullous have been reported.

Irreversible skin pigmentation (chrysiasis) can occur in sun-exposed areas after prolonged treatment with MYOCRISIN.

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.

### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

### 4.9 OVERDOSE

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.

Symptomatic treatment should be initiated in case of overdose.

Major skin lesions and serious blood disorders demand hospital admission. Skin reactions should be treated with systemic and topical antihistamines and corticosteroids. In case of overdose, chelation of gold by antidote treatments may be used. 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.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Gold preparations, ATC code: M01CB01

### Mechanism 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.

### 5.2 PHARMACOKINETIC PROPERTIES

#### Absorption

Gold is completely absorbed from an intramuscular injection of MYOCRISIN.

#### Distribution

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.

#### Elimination

Gold is subject to significant excretion in the urine and faeces.

### 5.3 PRECLINICAL SAFETY DATA

No additional pre-clinical data of relevance to the prescriber.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 LIST OF EXCIPIENTS

Phenylmercuric nitrate

Water for injections.

### 6.2 INCOMPATIBILITIES

Not applicable.

### 6.3 SHELF LIFE

36 months

### 6.4 SPECIAL PRECAUTIONS FOR STORAGE

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

### 6.5 NATURE AND CONTENTS OF CONTAINER

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

### 6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

No special requirements.

## 7 MEDICINE SCHEDULE

Prescription Medicine

## 8 SPONSOR

sanofi-aventis new zealand limited
Level 8, 56 Cawley Street
Ellerslie
Auckland
New Zealand

Toll Free Number (medical information): 0800 283 684

## 9 DATE OF FIRST APPROVAL

31 December 1969

## 10 DATE OF REVISION OF THE TEXT

31 May 2018

## Summary of changes

| Section changed | Summary of new information |
|---|---|
| All | Align with the Medsafe data sheet format including minor additions of text to meet requirements |
| 1 | Product name updated as part of reformatting |
| 2 | Updated to reflect TPDR , excipient with known effect added and reference to excipient list added |
| 3 | Pharmaceutical form added |
| 4.2 | Cross reference added |
| 4.3 | Contraindications re-worded and history of systemic lupus erythematosus added |
| 4.4 | Additional precautions added throughout section |
| 4.6 | Additional warning statement about avoiding pregnancy added. Cross reference to contraindications added<br>Lactation section re-worded |
| 4.8 | Additional Adverse Effects added throughout section<br>Statement added for reporting of suspected adverse reactions |
| 4.9 | Additional statements added about symptomatic treatment, hospital admission and chelation of gold.<br>Posisons information contact details added |
| 5.1 | Pharmacotherapeutic group and ATC code added |
| 5.3 | Statement added about pre-clinical safety data |
| 6.2 | Incompatibilty statement added |
| 6.3 | Shelf-life added |
| 6.5 | Nature of container added |
| 6.6 | Statement about precautions for disposal added |
| 8 | Telephone details added |
| 9 | Date of first approval added |