SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Myocrisin 100mg/ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5ml of solution for injection contains 50mg of Sodium aurothiomalate (100mg/ml).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Injection

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Myocrisin is used in the management of active progressive rheumatoid arthritis and progressive juvenile chronic arthritis especially if polyarticular or seropositive.

4.2 Posology and method of administration

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

Myocrisin should be administered only by deep intramuscular injection followed by gentle massage of the area. The patient should remain under medical observation for a period of 30 minutes after drug administration.

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 g (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 sign of remission occurs after this time other forms of treatment are to be considered.

**Elderly:**

There are no specific dosage recommendations. 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 1/10 or 1/5 of the full dose for 2-3 weeks. Continue weekly doses until signs of remission appear then increase the intervals between injections to two weeks. With full remission increase the interval to three then four weeks. In the absence of signs of remission after twenty weeks consider raising the dose slightly or changing to another therapy.

Treatment should be continued for six months. Response can be expected at the 300-500 mg level. If patients respond, maintenance therapy should be continued with the dosage administered over the previous 2-4 weeks, for 1-5 years.

### 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

Pregnancy (see section 4.6)

Myocrisin is contraindicated in patients with severe renal or hepatic disease, a history of blood dyscrasias, exfoliative dermatitis or systemic lupus erythematosus.

The absolute contraindications should be positively excluded before considering gold therapy.

### 4.4 Special warnings and precautions for use

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 ten
minutes following drug administration (see administration). If anaphylactoid effects are observed, treatment with Myocrisin should be discontinued (see section 4.8).

Myocrisin should be administered with extra caution in the elderly and in patients with a history of urticaria, eczema. Extra caution should also be exercised if phenylbutazone or oxyphenbutazone are administered concurrently. Myocrisin should be administered with extra caution in patients with a history of enterocolitis or pulmonary fibrosis. An annual x-ray is recommended and attention should be paid to unexplained breathlessness and dry cough.

Before starting treatment and again before each injection, the urine should be tested for protein, the skin inspected for rash and a full blood count performed, including a numerical platelet count (not an estimate) and the readings plotted. Blood dyscrasias are most likely to occur when between 400 mg and 1 g of gold have been given, or between the 10th and 20th week of treatment, but can also occur with much lower doses or after only 2-4 weeks of therapy (see section 4.8).

The presence of albuminuria, pruritus or rash, or an eosinophilia, are indications of developing toxicity (see section 4.8). Myocrisin should be withheld for one or two weeks until all signs have disappeared when the course may be restarted on a test dose followed by a decreased frequency of gold injections.

A complaint of 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 (see section 4.8). Every patient treated with Myocrisin should be warned to report immediately the appearance of pruritus, metallic taste, sore throat or tongue, stomatitis, buccal ulceration or easy bruising, purpura, epistaxis, bleeding gums, menorrhagia or diarrhoea (see section 4.8).

4.5 Interaction with other medicinal products and other forms of interaction

Concurrent gold administration may exacerbate aspirin-induced hepatic dysfunction. Caution should be exercised if phenylbutazone or oxyphenbutazone are administered concurrently.

Gold salts should not be used concomitantly with penicillamine.

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

4.6 Pregnancy and lactation

The safety of Myocrisin in the foetus and the new-born has not been established. Female patients receiving Myocrisin should be instructed to avoid pregnancy. Pregnant patients should not be treated with Myocrisin. Lactating mothers under treatment with Myocrisin excrete significant amounts of gold in their breast milk and should not breast feed their infants.

4.7 Effects on ability to drive and use machines
None.

## 4.8 Undesirable effects

The following CIOMS frequency rating is used, when applicable:

*Very common* ≥ 10%; *Common* ≥ 1 and < 10%; *Uncommon* ≥ 0.1 and < 1%; *Rare* ≥ 0.01 and < 0.1%; *Very rare* < 0.01%; *Not known* (cannot be estimated from available data).

<table>
<thead>
<tr>
<th>System organ class</th>
<th>Frequency</th>
<th>Preferred Term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Not known</td>
<td>Blood disorders including thrombocytopenia, pancytopenia, agranulocytosis, aplastic anaemia, leucopenia &amp; neutropenia have been reported (see section 4.4). Other indicators of developing toxicity could be the presence of eosinophilia (see section 4.4).</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Not known</td>
<td>Anaphylactic/Anaphylactoid reactions have been reported, symptoms of which may include weakness, flushing, hypotension, tachycardia, dyspnoea, palpitations, abdominal pain, shock and possibly collapse (see section 4.4).</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Very rare</td>
<td>Neurological manifestations of gold toxicity including very rare cases of peripheral neuropathy, Guillain-Barré syndrome and encephalopathy have been observed.</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Not known</td>
<td>Diffuse unilateral or bilateral pulmonary fibrosis very rarely occurs. This progressive condition usually responds to drug withdrawal and steroid therapy. An annual x-ray is recommended and attention should be paid to unexplained breathlessness and dry cough.</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Rare</td>
<td>A rare but severe form of enterocolitis has been described.</td>
</tr>
<tr>
<td>Hepatobiliary disorders</td>
<td>Rare</td>
<td>Hepatotoxicity with cholestatic jaundic is a rare complication which may occur early in the course of treatment. It subsides on withdrawing Myocrisin.</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Rare</td>
<td>Rare reports of alopecia exist</td>
</tr>
<tr>
<td></td>
<td>Not known</td>
<td>Severe skin reactions that have been reported include exfoliative dermatitis and bullous eruptions. Minor reactions, usually manifest as skin rashes and pruritus are the most frequent and commonly benign, but as such reactions may be the forerunners of severe gold toxicity they must never be treated lightly.</td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>Rare</td>
<td>Nephrotic syndrome has been rarely reported.</td>
</tr>
<tr>
<td></td>
<td>Not known</td>
<td>Other indicators of developing toxicity</td>
</tr>
</tbody>
</table>
could be the presence of albuminuria (see section 4.4).

| General disorders and administration site conditions | Not known | Vasomotor (nitritoid) reactions |
| Injury, poisoning and procedural conditions | Not known | Irreversible skin pigmentation (chrysiasis) can occur in sun-exposed areas after prolonged treatment with Myocrisin |

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme at: [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in the Google Play or Apple App Store.

### 4.9 Overdose

Minor side effects resolve spontaneously on withdrawal of Myocrisin. Symptomatic treatment of pruritus with antihistamines may be helpful. Major skin lesions and serious blood dyscrasias demand hospital admission when dimercaprol or penicillamine may be used to enhance gold excretion. Fresh blood and/or platelet transfusions, corticosteroids and androgenic steroids may be required in the management of severe blood dyscrasias.

### 5 PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties

The precise mode of action of sodium aurothiomalate is not yet known. Treatment with gold has been shown to be accompanied by a fall in ESR and C-reactive protein, an increase in serum histidine and sulphhydryl levels and a reduction in serum immunoglobulins, rheumatoid factor titres and Clq-binding activity.

Numerous experimental observations have been recorded including physico-chemical changes in collagen and interference with complement activation, gammaglobulin aggregation, prostaglandin biosynthesis, inhibition of cathepsin and production of superoxide radicals by activated polymophonuclear leukocytes.

#### 5.2 Pharmacokinetic properties

Sodium aurothiomalate is absorbed readily after intramuscular injection and becomes bound to plasma proteins. With doses of 50 mg weekly the steady-state serum concentration of gold is about 3 to 5 microgram per ml. It is widely distributed and accumulates in the body. Concentrations in synovial
fluid have been shown to be similar or slightly less than those in plasma. Sodium aurothiomalate is mainly excreted in the urine with smaller amounts in the faeces. The serum half-life of gold clearance is about 5 or 6 days but after a course of treatment, gold may be found in the urine for up to a year or more owing to its presence in deep body compartments.

Gold has been detected in the foetus following administration of sodium aurothiomalate to the mother. Gold has been detected in the breast fed child where the mother has received sodium aurothiomalate.

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

None known.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 25°C. Protect from light.

6.5 Nature and contents of container

Carton containing 10 sealed glass ampoules each containing 0.5ml injection solution.
6.6 Special precautions for disposal

None stated

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 04425/0389

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/09/1997 / 13/03/2003

10 DATE OF REVISION OF THE TEXT

27/02/2019