IRISH MEDICINES BOARD ACT 1995

MEDICINAL PRODUCTS(LICENSING AND SALE)REGULATIONS, 1998

(S.I. No.142 of 1998)

PA0040/068/005
Case No: 2030701

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

May & Baker Limited

RPR House, **50 Kings Hill Avenue**, **West Malling**, **Kent ME19 4AH**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Myocrisin Injection 50 mg (10% w/v)

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **31/01/2007** until **31/03/2008**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Myocrisin Injection 50mg (10%w/v)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium Aurothiomalate, 50 mg in 0.5 ml.

For excipients see 6.1.

3 PHARMACEUTICAL FORM

Solution for Injection
A pale yellow aqueous solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For use in the management of active progressive rheumatoid arthritis, including progressive juvenile rheumatoid arthritis especially if polyarticular or sero-positive. In some cases of chronic discoid lupus erythematosus unresponsive to anti-malarials a response may be obtained with this drug.

4.2 Posology and method of administration

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

Adults (including elderly):

An initial dose of 10mg should be given the first week followed by weekly doses of 50mg until signs of remission occur. At this point, 50mg doses should be given 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 100mg injections may be administered at weekly intervals. If no signs of remission occur after this time, other forms of treatment are to be considered.

Children:

Therapy should be initiated with low doses with gradual increments to the following maxima:

Of over 50kg b.w.	30mg
Of 20 – 50kg b.w.	20mg
Of less than 20kg b.w.	10mg

Dosage should be continued for a 6 months. If no improvement has occurred, therapy should be stopped. If improvement has occurred, maintenance dosage is given 2 - 4 weeks for up to 5 years.

4.3 Contraindications

Use in patients with systemic lupus, erythematosus, or with a history of blood dyscrasias, circulatory defects, or exfoliative dermatitis, or nephrotic syndrome, uncontrolled hypertensives.

Use in patients with moderate or severe renal or hepatic dysfunction, severe anaemia.

Use in patients who have developed blood dyscrasias, proteinaemia in excess of 30mg/100ml, a glomerular filtration rate (GFR) < 50ml/minute or anaphylactoid reaction or dermatoses during therapy.

4.4 Special warnings and precautions for use

Do not use darkened solutions (more than pale yellow).

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.

The use of gold therapy should be introduced under specialist supervision with careful investigation and selection of the patient with particular attention to skin, haematologic and renal states. Patients on therapy should be kept under regular clinical and laboratory surveillance to permit early detection of any adverse affects.

Adverse reactions such as mucosal ulceration dermatosis, evidence of bleeding or purpura pulmonary fibrosis, nephropathy, blood dyscrasia and aplastic anaemia demand the immediate cessation of therapy and the institution of appropriate active measures to control the effect. The Myocrisin should be withheld for one or two weeks until all signs have disappeared then the course can be restarted on a test dose followed by a decreased frequency of gold injections.

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.

Gold should be used with great caution in the elderly or in patients with urticaria, otitis or eczema.

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 400mg and 1 gram of gold have been given or between the 10th and 20th week of treatment but can also occur with much lower doses or after 2-4 weeks therapy.

Every patient treated with Myocrisin should be warned to report immediately the appearance of pruritis, metallic taste, sore throat or tongue, buccal ulceration or easy bruising, purpura, epistaxis, bleeding gums, menorrhagia or diarrhoea.

The presence of albuminuria, pruritis or rash of an eosinophilia, are indications of developing toxicity. Myocrisin should be withheld for one or two weeks until all signs have disappeared. The course can then be restarted on a test dose followed by a decreased frequency of gold injections.

The mechanism of excretion of gold and its nephrotic actions are still uncertain but there does not appear to be any marked reduction in renal function, although a few cases of severe damage are on record. Patients who develop ‘gold nephrosis’ may suffer proteinuria and oedema of ankles, feet, and eyelids accompanied by ‘nephrosis-type’ protein distribution on serum electrophoresis. The withdrawal of gold and administration of prednisolone will usually correct abnormalities. Anaphylactoid reaction, psychosis, peptic ulcer and fever are other reactions that have been associated with gold therapy. Myocrisin may be given in the presence of a trace protein, but if there is 30mg per 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.

4.5 Interaction with other medicinal products and other forms of interaction

1. Gold salts should be used with great caution in patients who are concurrently receiving other haemotoxic drugs such as phenylbutazone, penicillamine, anti-neoplastic agents or have recently had x-irradiation.

2. Dimercaprol, corticosteroids, anabolic steroids and occasionally penicillamine may be used as a treatment for adverse reactions to gold.

3. 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 Pregnancy and lactation

The drug accumulates in the placenta and concentrates also in the foetus, and also is excreted in the breast milk. The drug should not be used during pregnancy or lactation in women breast feeding infants. It has been shown to be teratogenic in animals. Safety to human foetus or neonate has not been established. Female patients should avoid pregnancy during treatment.

4.7 Effects on ability to drive and use machines

None when used as recommended.

4.8 Undesirable effects

Side effects include hypersensitivity, erythema multiforme, exfoliative dermatitis, alopecia, blood dyscrasias, proteinuria, dysguesia, fever, pruritus, and stomatitis. Colitis, toxic hepatitis, haematuria, peripheral neuritis and encephalitis and keratitis may occur.

Diffuse, unilateral or bilateral pulmonary fibrosis very rarely occurs. This progressive condition usually responds to drug withdrawal and steroid therapy. Annual chest x-ray is recommended and attention should be paid to unexplained breathlessness and dry cough.

Irreversible skin pigmentation can occur to sun-exposed areas after prolonged treatment with Myocrisin.

Neurological manifestations of gold toxicity including very rare cases of peripheral neuropathy, Guillain Barre Syndrome and encephalopathy have been observed.

4.9 Overdose

Minor side-effects resolve spontaneously on withdrawal of Myocrisin. Symptomatic treatment of pruritis 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

A gold compound readily absorbed after intramuscular injection and used for its anti-inflammatory effect.

5.2 Pharmacokinetic properties

After intramuscular injection sodium aurothiomalate is absorbed and becomes bound to plasma proteins. With doses of 50mg weekly the steady-state serum concentration of gold is about 3 to 5 micrograms per ml. It is strongly protein

bound and concentrates in the kidney, liver and spleen. Excretion is mainly via the urine with a serum half-life of 5-6 days. Prolonged treatment leads to the accumulation of gold deposits in various organs with an extended period of elimination.

5.3 Preclinical safety data

There is no other information available which could be of relevance to the prescriber in recognising the safety profile of Myocrisin and which is not included in the relevant sections of this SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenylmercuric nitrate
Water for injection

6.2 Incompatibilities

None.

6.3 Shelf Life

Unopened 3 years.
Once opened the product should be used immediately.

6.4 Special precautions for storage

Do not store above 25° C.
Store in the original container.

6.5 Nature and contents of container

Myocrisin is presented in Type I glass ampoules, heat sealed, with snap ring. Ampoules are packed in boxes of 10.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

This product should not be used if the solution is discoloured.

7 MARKETING AUTHORISATION HOLDER

May & Baker Limited
RPR House
50 Kings Hill Avenue
West Malling
Kent ME19 4AH
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 40/68/5

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 April 1983

Date of last renewal: 01 April 2003

10 DATE OF REVISION OF THE TEXT

April 2005