Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ridaura Tiltab 3mg Film-coated Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 3 mg auranofin.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

Square, bevel-edged, pale yellow, film-coated tablets with raised domes on both sides.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Ridaura is an orally active gold preparation. 'Ridaura' is indicated for the treatment of adults with active progressive rheumatoid arthritis only when non-steroidal anti-inflammatory drugs have been found to be inadequate alone to control the disease, ie. when second line therapy is required. In patients with adult rheumatoid arthritis Ridaura has been shown to reduce disease activity reflected by synovitis, associated symptoms, and appropriate laboratory parameters. Gold can not reverse structural damage joints caused by previous disease. Ridaura does not produce an immediate response and therapeutic effects may be seen after three to six months of treatment.

4.2 Posology and method of administration

Adults only:

The usual starting dose is one 3 mg tablet twice a day with breakfast and the evening meal. If this is well tolerated a single daily dose may be given as two 3 mg tablets with breakfast or the evening meal.

If there is no satisfactory response as Ridaura is a slow acting drug, after four to six months, the dosage may be increased to one tablet three times a day with meals (9 mg a day) for a short period.
If response remains inadequate after a three months trial of 9mg daily, Ridaura therapy should be discontinued.
Safety at dosages exceeding 9mg daily has not been studied.

Absorption of gold from 'Ridaura' tablets is rapid but incomplete. Although mean blood levels are proportional to dose, correlation between blood gold levels and safety or efficacy has been established. Dosage adjustments should theref depend on monitoring clinical response and adverse events rather than on monitoring blood gold concentrations..

Anti-inflammatory drugs and analgesics should be prescribed as necessary with 'Ridaura' as its effect may not be clinically manifest for several months.

Elderly:

Dosages as above. As with all drugs, extra caution should be undertaken with administration to the elderly.

Administration

Oral.

4.3 Contraindications

Although not necessarily reported in association with 'Ridaura', do not use in patients with a history of any of the following gold-induced disorders: necrotizing enterocolitis, pulmonary fibrosis, exfoliative dermatitis, bone marrow aplasia or other severe blood dyscrasias or toxicity to other heavy metals.

Use should also be avoided in progressive renal disease (including nephrotic syndrome), with proteinuria of more than 30 mg/100 ml, severe hepatic disease, in systemic lupus erythematosus, in patients with a history of or existing inflammatory bowel disease, in patients on other potentially haemotoxic drugs such as penicillamine or phenylbutazone or in patients who have recently received therapeutic X-irradiation.

'Ridaura' should not be used in pregnancy.

'Ridaura should not be used in patients with hypersensitivity to gold salts or other heavy metals.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.4 Special warnings and precautions for use

Use with caution in patients with any degree of renal impairment or hepatic dysfunction, inflammatory bowel disease, rash or history of bone marrow depression. Use with caution in elderly patients; also in those with a history of allergic skin disease. The effect of the drug on immuno-responsiveness is as yet uncertain.

The use of gold therapy should be introduced under specialist supervision. Close monitoring is essential. Full blood count with differential and platelet counts which should be plotted, and tests for urinary protein, must be performed prior to 'Ridaura' therapy and at least monthly thereafter.

Patients with gastrointestinal symptoms, with rash or pruritis (which may precede rash), or with stomatitis or a metallic taste in the mouth (which may precede stomatitis), should also be closely monitored as such symptoms may indicate a need for modification of dosage or withdrawal.

Prior to initiating treatment, patients must be advised of the potential side-effects associated with 'Ridaura'. They should be warned to report promptly any unusual symptoms or signs during treatment, such as pruritis, rash, metallic taste, sore throat or tongue, mouth ulceration, easy bruising, purpura, epistaxis, bleeding gums, menorrhagia or diarrhoea.

Gold has been shown to be carcinogenic in rodents although there was no evidence of carcinogenicity in seven-year dog studies.

Pulmonary fibrosis may rarely occur and chest X-ray is recommended at least annually.

The occurrence of purpura, ecchymoses or petechia would suggest the presence of thrombocytopenia and may indicate a need for additional platelet count determinations.

Ridaura should be withdrawn if the platelet count falls below 100,000/mm^3 or if signs and symptoms suggestive or thrombocytopenia, leucopenia and aplastic anaemia occur.

Patients should be cautioned to minimise exposure to ultraviolet light.

Enterocolitis is a rare but potentially serious side effect, the development of diarrhoea with rectal bleeding or rectal bleeding alone unless rapidly explained otherwise mandates the immediate cessation of the therapy. Patients should be warned to seek medical advice as soon as possible if they develop these symptoms.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant therapy with metal antagonists and potentially nephrotoxic or haemotoxic drugs should be administered with caution. Such drugs include penicillamine, aminoglycosides, amphotericin B, penicillins, phenylbutazone, phenytoin, sulfonamides, NSAIDs, acyclovir and alcohol.

Drugs affecting GI motility and those which are highly protein-bound may alter the absorption and binding, respectively, of auranofin.

Periodic theophylline serum determinations are advised until further studies provide the necessary clarification about the kinetic profile of theophylline in patients taking concomitant steroids and gold salts.

4.6 Pregnancy and lactation

Gold is teratogenic in some animal species. 'Ridaura' should not be used in pregnancy. Women of child-bearing potential should not be treated with 'Ridaura' without full consideration of the benefits of treatment against the potential risk of teratogenicity. Women of child-bearing potential should practise effective contraception during treatment and for at least six months after; patients should be fully informed of the teratogenic risk, and termination of any pregnancy occurring during treatment should be considered in view of the possibility of foetal malformation. If women are to be treated post-partum with 'Ridaura', breast feeding should be avoided.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Adverse reactions can occur throughout treatment with 'Ridaura', although the highest incidence can be expected during the first six months of treatment.

The most common reaction to 'Ridaura' is diarrhoea or loose stools. Occurring in about 30% of patients according to the literature. Nausea may be present, and abdominal pain or other gastrointestinal symptoms have been reported alone or in association. These usually resolve if dosage is temporarily reduced, e.g. from 6 mg to 3 mg a day, but if it is necessary to stop treatment, it can sometimes be started again at a lower dosage without any further problem.

About one patient in 20 will be unable to tolerate 'Ridaura' because of diarrhoea. Ulcerative enterocolitis has been very rarely reported (<0.01%), as with all gold-containing drugs. Therefore patients with gastrointestinal symptoms should be carefully monitored for the appearance of gastrointestinal bleeding and treatment stopped if this occurs.

Blood and lymphatic system:	
Blood dyscrasias including leucopenia*, granulocytopenia and thrombocytopenia*, anaemia, eosinophilia	Common (>1/100, <1/10)
Agranulocytosis, aplastic anaemia*, red cell aplasia	Very rare (<1/10,000)
Nervous system disorders:	
Headache	Uncommon (>1/1000, <1/100)
Peripheral neuropathy, Dizziness	Very rare (<1/10,000)
Eye disorders	
Conjunctivitis	Common (>1/100, <1/10)
Gold deposits in the lens/corneas	Very rare (<1/10,000)
Respiratory, thoracic and Mediastinal disorders:	
Interstitial pneumonitis	Rare (>1/10,000, <1/1,000)
Pulmonary fibrosis	Very rare (<1/10,000)
Gastrointestinal disorders	
Diarrhoea or loose stools	Very Common (>1/10)
Oral mucous membrane disorder and stomatitis, disturbed taste	Uncommon (>1/1000, <1/100)
Nausea and vomiting, abdominal pain	Uncommon (>1/1000, <1/100)
Ulcerative enterocolitis	Very rare (<1/10,000)
Skin and subcutaneous tissue disorders	
Rashes and pruritis	Very Common (>1/10)
Exfoliative dermatitis and alopecia	Very rare (<1/10,000)
Renal and urinary disorders	
Proteinuria	Common (>1/100,<1/10)
Glomerular disease/nephritic syndrome/membranous glomerulonephritis	Very rare (<1/10,000)
Investigations	
Decrease in haemoglobin Decrease in haematocrit Changes in liver function Changes in renal function	Common (>1/100,<1/10)

The frequencies are taken from adverse events reported in controlled studies and post-marketing experience.

Post-Marketing information-

Treatment with Ridaura should be stopped in cases of persistent rash, especially if accompanied by pruritus. In cases of clinically significant proteinuria treatment with Ridaura should be stopped promptly. Treatment may be restarted after the proteinuria has cleared, however, under close supervision in patients who have experienced only minimal proteinuria.

Transient decreases in haemoglobin or haematocrit early in treatment have been reported. Occasional decreases in white blood counts have been reported during Ridaura treatment.
There have been some reports if gold deposits in the lens or corneas of patients treated with ridaura. These deposits have not led to any eye disorders or any degree of visual impairment.

4.9 Overdose

'Ridaura' overdosage experience is limited. One patient who took 27 mg 'Ridaura' daily for 10 days developed an encephalopathy and peripheral neuropathy. 'Ridaura' was discontinued and the patient eventually recovered.

In case of acute overdosage, immediate induction of vomiting or gastric lavage and appropriate supportive therapy are recommended.

Chelating agents (such as BAL) have been used with injectable gold and may be considered for 'Ridaura' overdosage, although there has been no specific experience with 'Ridaura'.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: M01CB03

'Ridaura' is an orally active gold preparation which may modify the disease process of rheumatoid arthritis. It does not have immediate anti-inflammatory or analgesic properties. It’s a slow acting immunomodulating agent.

5.2 Pharmacokinetic properties

About 20-30% of the gold in a dose of 'Ridaura' is absorbed and although there is considerable variation in absorption this variability is less than that seen with parenteral gold.

Steady state blood concentrations are achieved 8 to12 weeks after the start of treatment with 'Ridaura' are on average 5-10 times less than those following parenteral gold and do not correlate with clinical response or adverse events.

About 70% of gold administered in 'Ridaura' appears in the faeces during the first week following a single dose, and at six months after dosing less than 1% of the administered dose is retained in the body, in contrast to around 30% of a dose of gold given parenterally.

In contrast to injectable gold, which does not become cell-associated, 40% of the gold in the blood of 'Ridaura'-treated patients is associated with blood cells. The metabolism of 'Ridaura' is not fully understood, although it is clear from both animal studies and *in vitro* studies with human blood that both the sulphur and phosphorus ligands of 'Ridaura' are rapidly dissociated from the gold.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Microcrystalline cellulose
Maize starch
Sodium starch glycolate Type A
Magnesium stearate
Hypromellose
Propylene glycol
Titanium dioxide (E171)
Yellow iron oxide (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

5 years.

6.4 Special precautions for storage

Do not store above 25ºC. Store in the original container.

6.5 Nature and contents of container

White HDPE bottle, with a wadless polypropylene screw cap, containing 60 tablets.

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

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Goldshield Pharmaceuticals Limited,
NLA Tower,
12-16 Addiscombe Road,
Croydon CR0 0XT,
England.

8 MARKETING AUTHORISATION NUMBER

PA 0899/011/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 25 January 2005

10 DATE OF REVISION OF THE TEXT

October 2008