**Gastrointestinal Reactions:** Gastrointestinal reactions reported with gold therapy include diarrhea, loose stools, nausea, vomiting, anorexia, and abdominal cramps. The most common reaction to RIDAURA is diarrhea in 13% of patients. The second most common reaction is vomiting reported in approximately 12% of patients. 6% of the patients is it necessary to discontinue RIDAURA (auranofin) permanently.

**Cutaneous Reactions:** Dermatitis is the most common reaction to injectable gold therapy, and the second most common reaction to RIDAURA. Any eruption, especially if pruritic, that develops during treatment should be considered a gold reaction until proven otherwise. Pruritis often occurs before dermatitis becomes apparent, and therefore should be considered a warning signal of a cutaneous reaction. Gold dermatitis may be aggravated by exposure to sunlight or an acidic rash may develop. The most serious form of cutaneous reaction reported with injectable gold is generalized exfoliative dermatitis.

**Mucous Membrane Reactions:** Stomatitis, another common gold reaction, may be manifested by shallow ulcers on the buccal membranes, on the palate or in the pharynx. Stomatitis may occur as the only adverse reaction or with a dermatitis. Sometimes diffuse glossitis or gingivitis develops. A metallic taste may precede these oral mucous membrane reactions and should be considered a warning signal.

**Renal Reactions:** Gold can produce a nephrotic syndrome or glomerulitis with proteinuria and hematuria. These renal reactions are usually relatively mild and subside completely if recognized early and treatment is discontinued. They may become severe and chronic if treatment is continued after the onset of the reaction. Therefore it is important to perform urinalyses regularly and to discontinue treatment promptly if proteinuria or hematuria develops.

**Hematologic Reactions:** Blood dyscrasias including leukopenia, granulocytopenia, thrombocytopenia and aplastic anemia have all been reported as reactions to injectable gold and RIDAURA. These reactions may occur separately or in combination at anytime during treatment. Because they have potentially serious consequences, blood dyscrasias should be constantly watched for through regular monitoring (at least monthly) of the formed elements of the blood throughout treatment.  

**Miscellaneous Reactions:** Rare reactions attributed to gold include cholestatic jaundice; gold bronchitis and interstitial pneumonia; and fibrosis; peripheral neurophy; partial or complete hair loss; fever.  

**Information for Patients:** Patients should be advised of the possibility of toxicity from RIDAURA and of the signs and symptoms that they should report promptly. (Patient Information sheets are available.)
Women of childbearing potential should be warned of the potential risks of RIDAURA therapy during pregnancy (See PRECAU-
TIONS—Pregnancy). Laboratory Tests: CBC with differential, platelet count, urinalysis, and renal and liver function tests should be performed prior to RIDAURA (auranofin) therapy to establish a baseline and to identify any preexisting conditions.

CBC with differential, platelet count and uri-

nalysis should then be monitored at least monthly; other parameters should be moni-
tored as appropriate.

Drug Interactions: In a single patient-

report, there is the suggestion that concur-
rent administration of RIDAURA and pheny-

toin may have increased phenytoin blood

levels.

Carcinogenesis/Mutagenesis: In a 24-month study in rats, animals treated with auranofin at 0.1, 0.2 or 2.5 mg/kg/day orally (3, 8 or 21 times the human dose) or gold sodium thiomalate at 2 or 6 mg/kg injected twice weekly (4 or 12 times the human dose) were compared to untreated control animals.

There was a significant increase in the fre-

quency of renal tubular cell karyomegaly and cytomegaly and renal adenoma in the animals treated with 1.0 or 2.5 mg/kg/day of auranofin and 2 or 6 mg/kg twice weekly of gold sodium thiomalate. Malignant renal epithelial tumors were seen in the 1.0 mg/kg and the 2.5 mg/kg auran-
ofin and in the 6 mg/kg twice weekly gold sodium thiomalate-treated animals.

In a 12-month study, rats treated with aura-
ofin at 23 mg/kg/day (192 times the human dose) developed tumors of the renal tubular epithelium, whereas those treated with 3.6 mg/kg/day (30 times the human dose) did not.

In an 18-month study in mice given oral auranofin at doses of 1, 3 and 9 mg/kg/day, 8, 24 and 72 times the human dose, there was no statistically significant increase above controls in the instances of tumors. In the mouse lymphoma forward mutation assay, auranofin at high concentrations (313 to 700 ng/ml) induced increases in the mutation frequencies in the presence of a rat liver microsomal preparation. Auranofin pro-
duced no mutation effects in the Ames test (Salmonella), in the in vitro assay (Forward and Reverse Mutation Induction Assay with Saccharomyces), in the in vitro transfor-
mation of BALB/3T3 cell mouse assay or in the Dominant Lethal Assay.

Pregnancy: Teratogenic Effects—Pregnancy Category C. Use of RIDAURA (auranofin) by pregnant women is not recommended. Furthermore, women of childbearing poten-
tial should be warned of the potential risks of RIDAURA therapy during pregnancy. (See below.)

Pregnant animals given auranofin at doses of 0.5, 3 or 6 mg/kg/day (42 to 50 times the human dose) had impaired food intake, decreased maternal weights, decreased fetal weights and an increase above controls in the incidence of resorptions, abor-
tions and congenital abnormalities, mainly abdominal defects such as gastroschisis and umbilical hernia.

Pregnant rats given auranofin at a dose of 5 mg/kg/day (42 times the human dose) had an increase above controls in the incidence of resorptions and a decrease in litter size and weight linked to maternal toxicity. No such effects were found in rats given 2.5 mg/kg/day (21 times the human dose).

Pregnant mice given auranofin at a dose of 5 mg/kg/day (42 times the human dose) had no teratogenic effects.

There are no adequate and well-controlled RIDAURA studies in pregnant women.

Nursing Mothers: Nursing during RIDAURA therapy is not recommended. Following auranofin administration to rats and mice, gold is excreted in milk. Following the administration of injectable gold, gold appears in the milk of nursing women; human data on auranofin is not available.

Pediatric Use: RIDAURA (auranofin) is not recommended for use in pediatric patients because its safety and effectiveness have not been established.

ADVERSE REACTIONS

The adverse reactions incidences listed below are based on observations of 1) 4,784 RIDAURA-treated patients in clinical trials (2,474 U.S., 2,310 foreign), of whom 2,729 were treated more than one year and 573 for more than three years; and 2) post-
m K

marketing experience. The highest inci-
dence is during the first six months of treat-
ment; however, reactions can occur after many months of therapy. With rare excep-
tions, all patients were on concomitant non-
steroidal anti-inflammatory therapy; some of them were also taking low dosages of corticosteroids.

Reactions occurring in more than

1% of RIDAURA-treated patients

Gastrointestinal: loose stools or diarrhea (47%); abdominal pain (14%); nausea with or without vomiting (10%); constipation; anorexia; flatulence; dyspepsia; dysgeusia.

Dermatological: rash (24%); pruritus (17%); hair loss; urticaria.

Mucous Membrane: stomatitis (13%); conjunctivitis†; glossitis. 

Hematological: anemia; leukopenia; thrombocytopenia; eosinophilia.

Renal: proteinuria†; hematuria.

Hepatic: elevated liver enzymes.

*Reactions marked with an asterisk occurred in 0.1-1% of the patients. The other reactions listed in occurred in

Reactions occurring in less than 1% of RIDAURA-treated patients

Gastrointestinal: dysphagia, gastrointestinal bleeding†, melena†, positive stool for occult blood†, ulcerative enterocolitis.

Dermatological: angioedema.

Mucous Membrane: gingivitis†.

Hematological: aplastic anemia; neutrope-
ia†; agranulocytosis; pure red cell aplasia; pancytopenia.

Hepatic: jaundice.

Respiratory: interstitial pneumonitis.

Neurological: peripheral neuropathy.

Ocular: gold deposits in the lens or cornea unassociated clinically with eye disorders or visual impairment.

Reactions marked with a dagger occurred in 0.1-1% of the patients. The other reactions listed occurred in less than 0.1%.

Reactions reported with injectable gold preparations, but not with RIDAURA (auranofin) (based on clinical trials and on post-
marketing experience)

Cutaneous Reactions: generalized exfoli-
ative dermatitis.

Incidence of Adverse Reactions for Specific Categories—18 Comparative Trials

<table>
<thead>
<tr>
<th>Category</th>
<th>RIDAURA (445 patients)</th>
<th>Injectable Gold (449 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinuria</td>
<td>0.9%</td>
<td>5.4%</td>
</tr>
<tr>
<td>Rash</td>
<td>28%</td>
<td>39%</td>
</tr>
<tr>
<td>Nausea</td>
<td>43%</td>
<td>19%</td>
</tr>
<tr>
<td>Constipation</td>
<td>13%</td>
<td>16%</td>
</tr>
<tr>
<td>Anemia</td>
<td>4%</td>
<td>2%</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>1%</td>
<td>2%</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>2%</td>
<td>2.2%</td>
</tr>
<tr>
<td>Elevated liver function tests</td>
<td>1.9%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>1%</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

OVERDOSAGE

The acute oral LD 50 for auranofin is 310 mg/kg in adult mice and 265 mg/kg in adult rats. The minimum lethal dose in rats is 30 mg/kg.

In case of acute overdosage, immediate induction of emesis or gastric lavage and appropriate supportive therapy are recom-

mended.

RIDAURA overdosage experience is limit-
ed. A 50-year-old female, previously on 6 mg RIDAURA daily, took 2 mg of the injectable agent (234 mg gold) daily for 10 days and developed an encephalopathy and peripheral neuropathy. RIDAURA was discontinued and she even-
tually recovered.

There has been no experience with treating RIDAURA overdosage with modalities such as chelating agents. However, they have been used with injectable gold and may be considered for RIDAURA overdosage.

DOSAGE AND ADMINISTRATION

Usual Adult Dosage: The usual adult dosage of RIDAURA (auranofin) is 4 mg daily, given either as 3 mg twice daily or 6 mg once daily. Initiation of therapy at dosages exceeding 6 mg daily is not rec-

mended because it is associated with an increased incidence of diarrrhea. A response is inadequate after six months, an increase to 9 mg (3 mg three times daily) may be tol-

erated. If response remains inadequate after a three-month trial of 9 mg daily, RIDAURA therapy should be discontinued. Safety at dosages exceeding 9 mg daily has not been studied.

Transferring from Injectable Gold: In con-
trolled clinical studies, patients on injectable gold have been transferred to RIDAURA (auranofin) by discontinuing the injectable agent and starting oral therapy with RIDAURA, 4 mg daily. When patients are transferred to RIDAURA, they should be informed of its adverse reaction profile, in particular the gastrointestinal reactions. (See PRECAU-
TIONS—Information for Patients.) At six months, control of disease activity of patients transferred to RIDAURA and those maintained on the injectable agent was not different. Data beyond six months are not available.

HOW SUPPLIED

Capsules, containing 3 mg auranofin, in bottles of 60.

NDC: 54766-093-06

STORAGE AND HANDLING

Store between 15° and 30°C (59° and 86° F). Dispense in a tight, light-resistant container.

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Distributed by:

Sebela Pharmaceuticals Inc.

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Item Code

Description

Customer

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NDC 54766-093-06