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Cuprimine (Penicillamine)

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Penicillamine is a drug with a high incidence of untoward reactions, some of which are potentially fatal. Therefore, it is mandatory that patients receiving
) . **PRECAUTIONS** and **WARNINGS**penicillamine therapy remain under close medical supervision throughout the period of drug administration (see

Reported incidences (%) for the most commonly occurring adverse reactions in rheumatoid arthritis patients are noted, based on 17 representative clinical trials
reported in the literature (1270 patients).

), and drug eruptions which may be accompanied by fever, arthralgia, or **WARNINGS** — Generalized pruritus, early and late rashes (5%), pemphigus (see **Allergic**
) . Some patients may show a lupus erythematosus-like syndrome similar to drug-induced **PRECAUTIONS** and **WARNINGS**lymphadenopathy have occurred (see
) .**PRECAUTIONS**lupus produced by other pharmacological agents (see

Urticaria and exfoliative dermatitis have occurred.

Thyroiditis has been reported; hypoglycemia in association with anti-insulin antibodies has been reported. These reactions are extremely rare.

) .**DOSAGE AND ADMINISTRATION** Some patients may develop a migratory polyarthralgia, often with objective synovitis (see

— Anorexia, epigastric pain, nausea, vomiting, or occasional diarrhea may occur (17%). **Gastrointestinal**

Isolated cases of reactivated peptic ulcer have occurred, as have hepatic dysfunction including hepatic failure, and pancreatitis. Intrahepatic cholestasis and toxic
hepatitis have been reported rarely. There have been a few reports of increased serum alkaline phosphatase, lactic dehydrogenase, and positive cephalin
flocculation and thymol turbidity tests.

Some patients may report a blunting, diminution, or total loss of taste perception (12%); or may develop oral ulcerations. Although rare, cheilosis, glossitis, and
) .**PRECAUTIONS**gingivostomatitis have been reported (see

Gastrointestinal side effects are usually reversible following cessation of therapy.

) . Leukopenia (2%) and thrombocytopenia (4%) have occurred. Fatalities **WARNINGS** — Penicillamine can cause bone marrow depression (see **Hematological**
have been reported as a result of thrombocytopenia, agranulocytosis, aplastic anemia, and sideroblastic anemia.

Thrombotic thrombocytopenic purpura, hemolytic anemia, red cell aplasia, monocytosis, leukocytosis, eosinophilia, and thrombocytosis have also been reported.

— Patients on penicillamine therapy may develop proteinuria (6%) and/or hematuria which, in some, may progress to the development of the nephrotic **Renal**
) . Renal failure has been reported.**WARNINGS** syndrome as a result of an immune complex membranous glomerulopathy (see

— Tinnitus, optic neuritis and peripheral sensory and motor neuropathies (including polyradiculoneuropathy, i.e., Guillain-Barré syndrome) **Central Nervous System**
have been reported. Muscular weakness may or may not occur with the peripheral neuropathies. Visual and psychic disturbances; mental disorders; and agitation
and anxiety have been reported.

); dystonia.**WARNINGS** — Myasthenia gravis (see **Neuromuscular**

) ; falling hair or alopecia; lichen planus; **PRECAUTIONS** — Adverse reactions that have been reported rarely include thrombophlebitis; hyperpyrexia (see **Other**
polymyositis; dermatomyositis; mammary hyperplasia; elastosis perforans serpiginosa; toxic epidermal necrolysis; anetoderma (cutaneous macular atrophy); and
) . Vasculitis, including fatal **WARNINGS**Goodpasture's syndrome, a severe and ultimately fatal glomerulonephritis associated with intra-alveolar hemorrhage (see
renal vasculitis, has also been reported. Allergic alveolitis, obliterative bronchiolitis, interstitial pneumonitis and pulmonary fibrosis have been reported in patients with
severe rheumatoid arthritis, some of whom were receiving penicillamine. Bronchial asthma also has been reported.

Increased skin friability, excessive wrinkling of skin, and development of small white papules at venipuncture and surgical sites have been reported
) ; yellow nail syndrome.**PRECAUTIONS**(see

The chelating action of the drug may cause increased excretion of other heavy metals such as zinc, mercury and lead.

There have been reports associating penicillamine with leukemia. However, circumstances involved in these reports are such that a cause and effect relationship to

the drug has not been established.