PENICILLAMIN caps:

CLASS: Chelating Agent

INDICATIONS: Treatment of Wilson's disease, cystinuria; adjunctive treatment of severe, active rheumatoid arthritis

Canadian labeling: Additional use (not in U.S. labeling): Treatment of chronic lead poisoning

AVAILABLE DOSAGE FROM THE HOSPITAL:

PENICILLAMIN 125MG CAP, PENICILLAMINE 250MG CAP, PENICILLIN V 125MG/5ML SUSP, PENICILLIN V 1.000.000 IU TAB

DOSAGE: Note: Dose reduction to 250 mg/day may be considered prior to surgical procedures. May resume normal recommended dosing post-operatively once wound healing is complete.

-Cystinuria: Oral: 1-4 g/day in 4 divided doses; usual dose: 2 g/day; initiation of therapy at 250 mg/day with gradual upward titration may reduce the risk of unwanted effects. Note: Adjust dose to limit cystine excretion to 100-200 mg/day (<100 mg/day with history of stone formation).

-Lead poisoning: Oral: Canadian labeling: 900-1500 mg/day in 3 divided doses for 1-2 weeks, then 750 mg/day in divided doses until blood lead concentrations <60 mcg/dL or urinary lead excretion <500 mcg/L for 2 consecutive months.

-Rheumatoid arthritis: Oral: Initial: 125-250 mg/day, may increase dose by 125-250 mg/day at 1- to 3-month intervals up to 1-1.5 g/day; discontinue in patients failing to improve after 3-4 months at these doses

-Wilson's disease: Oral: Note: Dose that results in an initial 24-hour urinary copper excretion >2 mg/day should be continued for ~3 months; maintenance dose defined by amount resulting in <10 mcg serum free copper/dL.

-Manufacturer labeling recommendations: 750-1500 mg/day in divided doses; maximum dose: 2000 mg/day. Note: Limit daily dose to 750 mg/day (U.S. labeling) or 1000 mg/day (Canadian labeling) in pregnant women; if planned caesarian, limit dose to 250 mg/day during the last 6 weeks of pregnancy and postoperatively until wound healing is complete.

-Alternate recommendations (unlabeled dosing): To increase tolerability, therapy may be initiated at 250-500 mg/day then titrated upward in 250 mg increments every 4-7 days; usual maintenance dose: 750-1000 mg/day in 2 divided doses; maximum: 1000-1500 mg/day in 2-4 divided doses. (American Association for the Study of Liver Diseases [AASLD] guidelines) (Roberts, 2008).

Geriatric

Therapy should be initiated at low end of dosing range and titrated upward cautiously. Refer to adult dosing.
Renal Impairment:

-Manufacturer labeling recommendations: No dosage adjustment provided in manufacturer’s labeling; however, the manufacturer labeling does suggest a cautious approach to dosing as this drug undergoes mainly renal elimination.

-Alternate recommendations:
  
  $Cl_{cr} < 50$ mL/minute: Avoid use (Aronoff, 2007)
  
  Hemodialysis: Dialyzable; Administer 33% of usual dose (Aronoff, 2007); a dosing decrease from 250 mg/day to 250 mg 3 times/week after dialysis has been suggested in the treatment of rheumatoid arthritis (Swarup, 2004).

Hepatic Impairment:

No dosage adjustment provided in manufacturer's labeling; however, only a small fraction is metabolized hepatically.

COMMON SIDE EFFECT:

Frequency not always defined and may vary by indication.

- Cardiovascular: Vasculitis
- Central nervous system: Anxiety, agitation, fever, Guillain-Barré syndrome, hyperpyrexia, psychiatric disturbances, worsening neurologic symptoms
- Dermatologic: Alopecia, cheilitis, dermatomyositis, drug eruptions, exfoliative dermatitis, lichen planus, pemphigus, pruritus, rash (early and late: 5%), skin friability increased, toxic epidermal necrolysis, urticaria, wrinkling (excessive), yellow nail syndrome
- Endocrine & metabolic: Hypoglycemia, thyroiditis
- Gastrointestinal: Diarrhea (17%), taste alteration (12%), anorexia, epigastric pain, gingivostomatitis, glossitis, nausea, oral ulcerations, pancreatitis, peptic ulcer reactivation, vomiting
- Hematologic: Thrombocytopenia (4%), leukopenia (2%), agranulocytosis, aplastic anemia, eosinophilia, hemolytic anemia, leukocytosis, mononucleosis, red cell aplasia, sideroblastic anemia, thrombotic thrombocytopenia purpura, thrombocytosis
- Hepatic: Alkaline phosphatase increased, hepatic failure, intrahepatic cholestasis, toxic hepatitis
- Local: Thrombophlebitis, white papules at venipuncture and surgical sites
- Neuromuscular & skeletal: Arthralgia, dystonia, myasthenia gravis, muscle weakness, neuropathies, polyarthralgia (migratory, often with objective synovitis), polymyositis
- Ocular: Diplopia, extraocular muscle weakness, optic neuritis, ptosis, visual disturbances
- Otic: Tinnitus
- Renal: Proteinuria (6%), Goodpasture's syndrome, hematuria, nephrotic syndrome, renal failure, renal vasculitis
- Respiratory: Asthma, interstitial pneumonitis, pulmonary fibrosis, obliterative bronchiolitis
- Miscellaneous: Allergic alveolitis, anetoderma, elastosis perforans serpiginosa, lupus-like syndrome, lactic dehydrogenase increased, lymphadenopathy, mammary hyperplasia, positive ANA test

PREGNANCY RISK FACTORS: D