Zinc acetate occurs as white crystals or granules, freely soluble in water and in boiling alcohol, and slightly soluble in alcohol.

GALZN® (Zinc Acetate) Capsules contain the equivalent of 25 or 50 mg of zinc, in addition to corn starch and magnesium stearate in gelatin capsules. The 25 mg capsule shells contain titanium dioxide and the 50 mg capsule shells contain titanium dioxide, methylparaben and propylparaben.

The active moiety in zinc acetate is zinc cation. Regardless of the ligand, zinc induces the production of metallothionein in the enterocyte, a protein that binds to excess copper, thereby preventing the reabsorption of endogenously secreted copper such as that from the gut, where copper enters the body. Zinc acetate is the correct formulation for this therapy because it is truly oral and because it has a higher zinc level than the zinc-glutathione complex found in penicillamine. Metallothionein is a non-enzymatic carrier system for the transport of copper in the body. The compound is produced in the mucosae of the gastrointestinal tract and, because of its intracellular localization, is cross-resistant with metallothionein produced in the liver. Since the biologic half-life of metallothionein is approximately 24 hours, the compound is continuously recycled by the enterocyte and relabeled with newly ingested copper.

In clinical practice, zinc acetate is used for the oral repletion therapy of Wilson's disease patients who have been initially treated with a chelating agent. The zinc acetate dosage is increased slowly, starting at 12.5 mg t.i.d. and increasing in 12.5 mg increments every 2 weeks until the desired effect is achieved. It is important to follow the recommended schedule of zinc acetate dosage adjustment because the major side effect of zinc therapy is nausea and vomiting. At the start of therapy, many patients are vomiting so frequently that it is necessary to begin with only one dose and to increase the dose slowly over the first month. The dosage is then increased to 25 mg t.i.d. after 4 weeks and to 50 mg t.i.d. after 8 weeks. The goal is to achieve net negative copper balance with or without further neurological improvement.

GALZN® (Zinc Acetate) Capsules, 25 mg, 50 mg, and 100 mg, contain FD&C Blue #1, FD&C Red #40, FD&C Yellow #10, FD&C Yellow #6, and titanium dioxide. The 25 mg capsule shells contain FD&C Blue #1, FD&C Red #40, FD&C Yellow #10, FD&C Yellow #6, and titanium dioxide. The 50 mg capsule shells contain FD&C Blue #1, FD&C Red #40, FD&C Yellow #10, FD&C Yellow #6, and titanium dioxide. The 100 mg capsule shells contain FD&C Blue #1, FD&C Red #40, FD&C Yellow #10, FD&C Yellow #6, and titanium dioxide.

Zinc Acetate Capsules are contraindicated in patients with known hypersensitivity to any of the components of the formulation.

Zinc acetate is not recommended for the initial therapy of symptomatic patients because of the delay required for zinc-induced increase in enterocyte metallothionein and blockade of copper uptake. Symptomatic patients should be treated initially, using chelating agents. During initial therapy, neurological deterioration may occur as stores of copper are mobilized. Once initial therapy has been completed, and neurologic improvement has been noted, the patient is clinically stable, maintenance treatment with zinc acetate can be considered, but patients may be continued on initial therapy as clinically indicated.
GALZIN® (Zinc Acetate) Capsules

distribution and metabolism, the physician must reinforce the need for compliance at each contact with the patient.

Monitoring Patients
Patients should be monitored primarily by assessment of existing signs and symptoms of Wilson's disease and 24-hour urine copper. Neuropsychiatric evaluations including speech as well as liver function tests including bilirubin and aminotransferases, should be done as appropriate.

The urinary excretion of copper is an accurate reflection of the body status of copper when patients are on chelation therapy. The clinician should be aware that urinary copper levels are usually increased with chelation therapy such as penicillamine or trientine. Adequate zinc therapy will eventually decrease urinary copper excretion to 125 μg per 24 hours or less. A significant trend upward indicates impending loss of copper control. The non-ceruloplasmin plasma copper (also known as free copper) is obtained by subtracting the ceruloplasmin-bound copper from the total plasma copper. Each mg of ceruloplasmin contains 3 μg of copper. In the United States study, non-ceruloplasmin plasma copper concentration was kept below 20 μg/dL. Urine and plasma for copper determinations should be collected in copper-free containers and assayed with equipment capable of accurately measuring copper at levels as low as 0.01 μg/mL.

An additional monitoring tool, if available, is the amount of radioactivity measured in the plasma 1 or 2 hours after orally administered 64Copper. In adequately controlled patients, the amount is less than 1.2% of the administered dose. The level of hepatic copper should not be used to manage therapy since it does not differentiate between potentially toxic free copper and safely bound copper.

In all treated patients, 24-hour urinary zinc levels may be a useful measure of compliance with the zinc acetate regimen.

Drug Interactions
Pharmacodynamic studies in Wilson's disease patients failed to demonstrate drug interactions between zinc acetate (50 mg t.i.d.) and ascorbic acid (1 g daily), penicillamine (1 g daily), and trientine (1 g daily). Therefore, precautions for zinc acetate effects do not seem necessary when Wilson's disease patients are taking vitamin C or approved chelating agents. However, no data are available to demonstrate that zinc acetate should be added to other drugs used for the treatment of Wilson's disease patients or is safe.

Nursing Mothers
Zinc does appear in breast milk and zinc-induced copper deficiency in the nursing baby may occur. Therefore, it is recommended that women on zinc therapy not nurse their babies.

Pediatric Use
Results of observations in a small number of patients in the two clinical trials suggest that pediatric patients aged 10 years and above can be adequately maintained at doses between 75 to 150 mg elemental zinc daily in divided doses. No patients below the age of 10 years have been studied.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Zinc acetate has not been tested for its carcinogenic potential in long-term animal studies, for its mutagenic potential or for its effect on fertility in animals. However, testing with other salts of zinc (zinc oxide, zinc stearate, zinc sulfate) did not reveal a mutagenicity potential in in vitro Ames assays, and human embryonic lung cell chromosomal aberration assay, and in vivo rat dominant lethal assay, and rat bone marrow cell chromosomal aberration assay.

Other salts of zinc (zinc oxide, zinc chloride, zinc citrate, zinc maleate, zinc carbonate, zinc sulfate) and pure zinc dust at oral doses up to 326 mg/Kg/day (18 times the recommended human dose based on body surface area) were found to have no effect on fertility and reproductive performance of male and female rats.

Pregnancy: Teratogenic Effects. Pregnancy Category A.
Studies in pregnant women have not shown that zinc acetate or zinc sulfate increases the risk of fetal abnormalities if administered during all trimesters of pregnancy. If this drug is used during pregnancy, the possibility of fetal harm appears remote. Because studies cannot rule out the possibility of harm, however, zinc acetate should be used during pregnancy only if clearly needed. While zinc acetate should be used during pregnancy only if clearly needed, copper toxicosis can develop during pregnancy if anti-copper therapy is stopped.

Oral teratology studies have been performed with zinc sulfate in pregnant rats at doses up to 42.5 mg/Kg/day (2 times the recommended human dose based on body surface area), mice at doses up to 30 mg/Kg/day (1 time the recommended human dose based on body surface area), rabbits at doses up to 60 mg/Kg/day (6 times the recommended human dose based on body surface area) and hamsters at doses up to 88 mg/Kg/day (5 times the recommended human dose based on body surface area) and have revealed no evidence of impaired fertility or harm to the fetus due to zinc sulfate. (See CLINICAL TRIALS).

ADVERSE REACTIONS
Clinical experience with zinc acetate has been limited. The following adverse reactions have been reported in patients with Wilson's disease on zinc therapy: a death following overdosage with zinc sulfate (See OVERDOSAGE) and a death in a patient with advanced liver disease and hemolytic crisis where zinc sulfate was used as initial treatment with mannitol irrigation; elevations of serum alkaline phosphatase, amylase and lipase lasting from weeks to months suggesting pancreatitis. The levels usually return to high normal within the first one or two years of zinc therapy.

Drug Abuse and Dependence
Zinc acetate has no potential for abuse, and it is not related pharmacologically or structurally to any other drug known to have abuse potential.

OVERDOSAGE
Acute oral overdosage with inorganic salts of zinc in humans is reported rarely. In the event of overdosage, the unabsorbed zinc salt should be removed from the stomach by lavage as quickly as possible. The plasma level of zinc should be measured, and heavy metal chelation therapy should be considered if the plasma level of zinc is elevated markedly (>1000 μg/dL). In addition, any signs or symptoms of toxicity should be treated as medically indicated.

One fatality associated with overdosage of zinc sulfate has been reported. The death of this adult woman followed the accidental ingestion of approximately 28 g of zinc sulfate. Death occurred on the fifth day after ingestion and was attributed to renal failure. Hemorrhagic pancreatitis and hyperglycemic coma resulted from the overdosage. The amount ingested was 500 mg/kg of zinc sulfate, a value that is in the same order of magnitude as that found to be lethal in animals.

DOSE AND ADMINISTRATION
The recommended adult dose is 50 mg as zinc three times daily (See CLINICAL TRIALS).

Since 25 mg t.i.d. is also an effective dose in children 10 years of age or older or in women who are pregnant, it may be advisable to use a dose of zinc to 25 mg three times a day, as long as the patient is compliant with therapy. The dose can be raised to 50 mg t.i.d. if monitoring indicates a lessening of control (see PRECAUTIONS: Monitoring Patients).

Patients should take zinc acetate on an empty stomach, at least one hour before or two to three hours after meals. For additional information, see PRECAUTIONS.

HOW SUPPLIED
GALZIN®, Zinc Acetate Capsules (25 mg zinc content) are #1 capsules with aqua blue opaque cap and body, imprinted “93-215.” Packaged in bottles of 250 (NDC 57844-215-52).

GALZIN®, Zinc Acetate Capsules (50 mg zinc content) are #1 capsules with orange opaque cap and body, imprinted “93-208.” Packaged in bottles of 250 (NDC 57844-208-52).

Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F). See USP Controlled Room Temperature. Dispense in a tight, light-resistant container as defined in the USP, with a child-resistant closure.

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