Extrapyramidal reactions are more common with the piperazine phenothiazines than other side effects. They can usually be controlled by concomitant use of antiparkinsonian agents and/or reduction in dosage. Other side effects associated with phenothiazines include other CNS effects (neuroleptic malignant syndrome), adverse behavioral effects, autonomic, allergic, endocrine, cardiovascular, dermatologic, hepatic, dermatologic and ocular effects.

Precautions
Severe, acute hypotension has occurred with the use of phenothiazines and is particularly likely to occur in patients with mitral insufficiency or pheochromocytoma. Rebound hypertension may occur in pheochromocytoma patients. Trilafon tablets should be used with caution in patients with psychic depression. Perphenazine may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks, such as driving a car or operating machinery. The possibility of suicide in depressed patients during treatment should be considered. Untoward reactions of perphenazine tend to be dose-related. Caution is suggested in the use of phenothiazine derivatives in breast cancer patients. The antiemetic effect of perphenazine may obscure signs of toxicity due to overdosage of other drugs, or render more difficult the diagnosis of disorders such as intestinal obstruction, Reye’s syndrome, brain tumor, or other encephalopathies. Patients on large doses of a phenothiazine who are undergoing surgery should be watched carefully for possible hypotensive phenomena. Moreover, reduced amounts of anesthetics or CNS depressants may be necessary. Trilafon tablets should be used with great caution in persons exposed to extreme heat or extreme cold. A significant unexplained rise in body temperature may suggest perphenazine intolerance, in which case therapy should be discontinued. Patients receiving phenothiazines should avoid...
undue exposure to sunlight. Phenothiazines should be used cautiously in patients with diminished renal function and in patients with respiratory impairment due to either acute pulmonary infections or to chronic respiratory disorders. With long-term therapy, the risk of liver damage, corneal and lenticular deposits, retinal changes, and irreversible dyskinesias should be considered. Periodic laboratory testing should be considered, especially during high-dose or prolonged therapy. Patients should be watched closely for renal hematologic and hepatic effects, especially between the fourth and tenth week of therapy. It white blood-cell depression occurs with significant depression of granulocytes, therapy should be discontinued. If abnormalities in hepatic or renal function tests occur, therapy should be discontinued. Drug Abuse and Dependence: In general, phenothiazines do not produce psychic dependence. However, following abrupt cessation of high-dose therapy, gastritis, nausea, vomiting, dizziness tremulousness and motor hyperactivity have been reported. These symptoms may be reduced by continuing concomitant antiparkinsonian agents for several weeks after phenothiazine withdrawal.

Pregnancy and Lactation
Perphenazine is excreted rapidly in breast milk.

Pediatric Usage: Safety and effectiveness in children less than 12 years of age have not been established.

Overdosage
Emergency treatment should be started immediately. Patients should be hospitalized as soon as possible. Concurrent ingestion of alcohol or other drugs or some other medical explanation for the patient's condition should be considered.

Symptoms: Perphenazine overdosage primarily involves the extrapyramidal system. Overdosage symptomatology is generally an extension of the many pharmacologic effects of perphenazine.

CNS depression progressing from drowsiness to stupor or coma with areflexia may occur. Patients with early or mild intoxication may experience restlessness, contusion and excitement. Other symptoms include hypotensive tachycardia, hypothermia, miosis, tremor, muscle twitching, spasm, rigidity or hypotonia, convulsions, difficulty in swallowing and breathing, cyanosis and respiratory and/or vasomotor collapse, possibly with sudden apnea.

Treatment: Treatment is symptomatic and supportive. Providing the patient is conscious, vomiting should be induced, even if emesis has occurred spontaneously. Pharmacologically-induced vomiting by the administration of ipecac syrup is the preferred method. Since ipecac has a central mode of emetic action in addition to its local gastric irritant properties, it should be noted that the central action may be blocked by the antiemetic effect of Trilafon tablets. The action of ipecac is facilitated by physical activity and by the concurrent administration of 240 to 360 milliliters of water. If emesis does not occur within 15 minutes, the dose of ipecac should be repeated. Precautions against aspiration must be taken, especially in infants and children. Following emesis, any drug remaining in the stomach may be adsorbed by activated charcoal administered as a slurry with water. If vomiting is unsuccessful or contraindicated, gastric lavage with physiologic saline solution should be performed, particularly in children. In adults, tap water can be used; however, as much as possible of the amount administered should be removed before the next instillation. Saline cathartics draw water into the bowel by osmosis and therefore may be valuable for their action in rapid dilution of bowel content. Standard measures (oxygen, intravenous fluids, corticosteroids) should be used to manage circulatory shock or metabolic acidosis. An open airway and adequate fluid intake should be maintained. Body temperature should be regulated. Hypothermia is expected, but severe hyperthermia may occur and must be treated vigorously. An electrocardiogram should be taken and close monitoring of cardiac function instituted...
agents that induce microsomal drug-metabolizing enzymes can enhance phenothiazine metabolism. Concurrent phenothiazine use with guanethidine in controlled hypertensive patients may result in exacerbation of hypertension after several days of dosing. Conversely, concurrent phenothiazine use with methyldopa and beta-adrenergic receptor blocking agents, administered for hypertension, may cause additive hypotensive effects.

Phenothiazines can block or reverse the pressor effects of epinephrine. Norepinephrine (levarterenol) or phenylephrine should be used to treat significant phenothiazine-induced hypotension.

Concurrent phenothiazine administration with levodopa to patients with Parkinson’s disease may result in a decreased antiparkinsonian response. Concomitant ingestion of oral phenothiazines and antacids, coffee, tea, cola beverages and pectinates should be avoided since this may decrease phenothiazine absorption.

**Dosage and Administration**

Dosage must be individualized and adjusted according to the severity of the disorder and the response obtained. Since extrapyramidal symptoms increase in frequency and severity with increased dosage, the lowest effective dose should be administered. These symptoms have disappeared upon reduction of dos-
age, withdrawal of medication or administration of an antiparkinsonian agent. After maximum therapeutic response is obtained, dosage may be decreased gradually to a minimum effective maintenance dose.

Anxiety and tension states: 2 to 4 mg as tablets three times daily, or one Trilafon tablet once daily.

Non-hospitalized psychotic patients: 4 to 8 mg as tablets three times daily initially; reduce as soon as possible to minimum effective dosage.

Hospitalized psychotic patients: 8 to 16 mg as tablets two to four times daily; avoid dosages in excess of 64 mg daily.

Severe nausea and vomiting in adults: 8 to 16 mg daily as tablets in divided doses. Occasionally 24 mg may be necessary; early dosage reduction is desirable.

Prolonged administration of doses exceeding 24 mg daily should be reserved for hospitalized patients or patients under continual observation.