Prochlorperazine is a phenothiazine derivative, designated chemically as 2-Chloro-10H-10-3-[4-(methyl-1-piperazinyl)propyl]phenothiazine with the following structural formula:

Each suppository, for rectal administration, contains 25 mg of prochlorperazine; with glycerin, glyceryl monopalmitate, glyceryl monostearate, hydrogenated coconut oil fatty acids and hydrogenated palm kernel oil fatty acids.

**CLINICAL PHARMACOLOGY**

Prochlorperazine is a proprerpazine derivative of phenothiazine. Like other phenothiazines, it exerts an antemetic effect through a depressant action on the chemoreceptor trigger zone.

**INDICATIONS AND USAGE**

Prochlorperazine 25 mg suppositories are indicated in the control of severe nausea and vomiting in adults.

**CONTRAINDICATIONS**

Do not use in comatose states or in the presence of large amounts of central nervous system depressants (alcohol, barbiturates, narcotics, etc.).

Do not use in pediatric surgery. Do not use in children under 2 years of age or under 20 lbs. Do not use in children for conditions for which dosage has not been established.

**WARNINGS**

**Increased Mortality in Elderly Patients with Dementia-Related Psychosis**

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. Compro® Prochlorperazine Suppositories USP is not approved for the treatment of patients with dementia-related psychosis (see WARNINGS).

**PRECAUTIONS AND ADVERSE REACTIONS**

**Neuroleptic Malignant Syndrome (NMS)**

The syndrome is characterized by hyperpyrexia, muscular rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis and cardiac dysrhythmias). The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc.) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary central nervous system (CNS) pathology. The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, 2) intensive symptomatic treatment and medical monitoring, and 3) treatment of any concomitant serious medical problems for which specific treatments are available. There is no general agreement about the management of NMS; however, it has been suggested that the discontinuation of antipsychotic medications may be appropriate and may relieve extrapyramidal symptoms and/or help control the serious underlying systemic illness.

If a patient requires antipsychotic drug treatment after recovery from NMS, the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored, since recurrences of NMS have been reported.

**Use in Pregnancy**

**Usage in Pregnancy:** Safety for the use of prochlorperazine during pregnancy has not been established. Therefore, prochlorperazine is not recommended for use in pregnant women except in cases of severe nausea and vomiting that are so serious and intolerable that, in the judgment of the physician, drug intervention is required and potential benefits outweigh possible hazards.

There have been reports of prolonged jaundice, extrapyramidal signs, hyperpyrexia or hyperpyrexia in newborn infants whose mothers received phenothiazines during pregnancy. Nursing Mothers: There is evidence that phenothiazines are excreted in the breast milk of nursing mothers.

**PRECAUTIONS**

**Leukopenia, Neutropenia and Agranulocytosis**

In clinical trial and postmarketing experience, events of leukopenia/neutropenia and granulocytopenia have been reported temporarily related to antipsychotic agents.

Possible risk factors for leukopenia/neutropenia include preexisting low white blood cell count (WBC) and history of drug-induced leukopenia/neutropenia. Patients with a pre-existing low WBC or a history of drug-induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy and should discontinue Compro® at the first sign of a decline in WBC in the absence of other causative factors.

**Patients with neutropenia** should be carefully monitored for fever or other symptoms or signs of infection and treated promptly if such symptoms or signs occur. Patients with severe neutropenia (absolute neutrophil count <1000/mm3) should discontinue Compro® and have their WBC followed up until recovery.

**Use in Patients with Impaired Hepatic Function**

Neuroleptic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately one third of human breast cancers are prolactin-dependent in vitro, a factor of potential importance. If the prescribing of these drugs is contemplated in a patient with a previously untreated breast cancer. Although disturbances such as galactorrhea, amenorrhea, gynecomastia and impotence have been reported, the clinical significance of elevated serum prolactin levels is unknown for most patients. An increase in mammary neoplasms with lactation found in rodents after chronic administration of neuroleptic drugs. Neither clinical nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorigenesis; the available evidence is considered too limited to be conclusive at this time.

**Chromosomal aberrations in spermatocytes and abnormal sperm have been demonstrated in rodents treated with certain neuroleptics.**

As with all drugs which exert an anticholinergic effect, and/or cause mydriasis, prochlorperazine should be used with caution in patients with glaucoma.

Because phenothiazines may interfere with thermoregulatory mechanisms, use with caution in persons who will be exposed to extreme heat.

Phenothiazines can diminish the effect of oral anticoagulants.

Phenothiazines can produce alpha-adrenergic blockade.

Thiazide diuretics may accentuate the orthostatic hypotension that may occur with phenothiazines.

Antihypertensive effects of guanethidine and related compounds may be counteracted when phenothiazines are used concomitantly.

Concomitant administration of propranolol with phenothiazines results in increased plasma levels of both.

Phenothiazines may lower the convulsive threshold; dosage adjustments of anticonvulsants may be necessary. Potentiation of anticonvulsant effects does not occur. However, it has been reported that phenothiazines may interfere with the metabolism of phenytoin and thus precipitate phenytoin serum levels.

The presence of phenothiazines may produce false-positive phenylketonuria (PKU) test results.
Long-Term Therapy: Given the likelihood that some patients exposed chronically to neuroleptics will develop tardive dyskinesia, it is advised that all patients in whom chronic use is contemplated be given, if possible, full information about this risk. Patients should be informed that if these symptoms occur they should be discontinued the use of these drugs and, if possible, full information about this risk. Patients should be informed that if these symptoms occur they should be discontinued at the low end of the dosing range, reflecting the frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy (see DOSE AND ADMINISTRATION).

ADVERSE REACTIONS

Neuroleptic Malignant Syndrome

Neuroleptic malignant syndrome, a potentially fatal condition, may occur in susceptible patients usually produces rapid reversal of symptoms. If necessary, the dosage of prochlorperazine or to discontinue the drug. After this treatment which patients are likely to develop the syndrome. The symptoms are persistent and in some patients appear to be irreversible. The syndrome is characterized by involuntary movements of the tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes these involuntary movements of the extremities are the only manifestations of tardive dyskinesia. A variant of tardive dyskinesia, tardive dystonia, has also been described. It has been reported that fine vermicular movements of the tongue may be an early sign of the syndrome and if the medication is stopped at that time the syndrome may not develop. Adverse Reactions Reported with Prochlorperazine or Phenothiazine Derivatives

Dystonic symptoms include: spasm of the neck muscles, sometimes progressing to tightness of the throat, swallowing difficulty, difficulty breathing, and/or protrusion of the tongue. These symptoms occur more frequently with drugs that have a piperazine side chain, and with greater severity with high potency and at higher doses of first generation antipsychotic drugs. An elevated risk of acute dystonia is observed in males and younger age groups.

Neuroleptic-Parkinsonism Syndrome: Symptoms include: mask-like facies; drooling; tremors; pillrolling motion; cogwheel rigidity; and shuffling gait. Reassurance and sedation are important. In most cases these symptoms are readily controlled when an anti-parkinsonism agent is administered concomitantly. Anti-parkinsonism agents should be used only when this is necessary. Generally, if the neuroleptic agent being used is not the primary cause of these symptoms, the dosage should be reduced or the drug discontinued. Should these symptoms occur in patients treated with anti-parkinsonism agents, it may be necessary to discontinue the neuroleptic agent. If hypotension occurs, the standard measures for managing circulatory shock should be initiated. If it is desirable to administer a vasodilator, norepinephrine bitartrate and phentylephrine hydrochloride are most suitable. Other pressor agents, including epinephrine, are not recommended because phenothiazine derivatives may reverse the usual elevating action of these agents and cause a further lowering of blood pressure. Limited experimental indicates that phenothiazines are not dialyzable.

DOSAGE AND ADMINISTRATION

Adults: Dosage should be increased more gradually in debilitated or emaciated patients. Elderly Patients: In general, dosages in the lower range are sufficient for most elderly patients. Since they appear to be more susceptible to hypotension and neuromuscular reactions, such patients should be observed closely. Dosage should be tailored to the individual, response carefully monitored and dosage adjusted accordingly. Dosage should be increased more gradually in elderly patients.

To Control Severe Nausea and Vomiting: Adjust dose to the response of the individual. At the lowest recommended dosage. Rectal Dose: 25 mg twice daily.

HOW SUPPLIED

Compr Prochlorperazine Suppositories USP 25 mg (for adults) are easy to open, and available in boxes of 12.

12’s - NDC 0002-0026-12

and at 20° to 25° C (68° to 77°F) [See USP Controlled Room Temperature].

Do not remove from wrapper until ready to use.