**CLINICAL PHARMACOLOGY:**

Perphenazine has actions at all levels of the central nervous system, particularly in the mesolimbic reward system, limbic pathways, and subcortical regions. Perphenazine is indicated for use in the treatment of schizophrenia and related disorders. Its main effect is to block dopamine receptors, thereby reducing the activity of the mesolimbic reward system and improving symptoms of schizophrenia.

**Pharmacokinetics:**

Perphenazine is rapidly absorbed after oral administration. The plasma elimination half-life of perphenazine was independent of dose and perphenazine concentrations were observed between 1 to 3 hours. The plasma elimination half-life of 7-hydroxyperphenazine was 10 to 25 hours. The oral bioavailability of perphenazine is about 80%. Its structural formula is:

![Structural formula of perphenazine]

**INTERACTIONS:**

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 developing movement disorders, including neuroleptic malignant syndrome (NMS) and tardive dyskinesia.

**SIDE EFFECTS:**

Some of the untoward actions of perphenazine tend to appear more frequently in patients with a previously diagnosed breast cancer. Although disturbances of consciousness have been reported, the safety of perphenazine in patients with dementia-related psychosis has not been established. Some patients who have received perphenazine products, their components, or related compounds have developed a syndrome consisting of potentially irreversible, involuntary movements (tardive dyskinesia).

**Neuroleptic Malignant Syndrome (NMS):**

Neuroleptic malignant syndrome (NMS) is a rare but potentially fatal syndrome characterized by hyperthermia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse, diaphoresis). The diagnosticevaluation of patients with this syndrome is complicated. Given these considerations, especially in the elderly, antipsychotics should not be used in patients with a history of NMS.

**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 developing movement disorders, including neuroleptic malignant syndrome (NMS) and tardive dyskinesia. This risk is greater for patients treated with higher doses for longer periods. Atypical antipsychotic drugs are associated with lower mortality in elderly patients with dementia-related psychosis compared to typical antipsychotic drugs.

**Usage in Pregnancy:**

The use of perphenazine during pregnancy is contraindicated if the potential benefits to the mother clearly outweigh the potential risks to the fetus. Perphenazine should be used during pregnancy only if the potential benefits to the mother clearly outweigh the potential risks to the fetus. Given these considerations, especially in the elderly, antipsychotics should not be used in patients with a history of NMS.

**Precautions:**

Cautions should be observed in giving it to patients who have access to large quantities of this drug, and until significant remission occurs. This type of patient should not have access to large quantities of this drug.

**Lactation:**

Perphenazine is excreted in breast milk. Breastfeeding is not recommended for patients receiving perphenazine.

**Pediatric Use:**

Safety and effectiveness in pediatric patients have not been established.

**Drug Interactions:**

The use of alcohol should be avoided, since additive effects and hypotension may occur. Since phenothiazines and central nervous system depressants (opiates, barbiturates) may potentiate the hypotensive effects of perphenazine, patients should be observed closely during the initiation of treatment with perphenazine. Phenytoin, carbamazepine, or other anticonvulsant agents may increase the plasma levels of perphenazine when given concomitantly. If these drugs are used concomitantly, the dose of perphenazine should be reduced. The use of anticholinergic drugs with perphenazine should be avoided, since additive anticholinergic effects may occur.

**Overdosage:**

Overdosage of perphenazine may result in drowsiness, ataxia, hypotension, and extrapyramidal symptoms. Supportive measures should be employed, and if necessary, specific treatment should be given. Specific treatment of overdose may include hemodialysis, forced diuresis, or the use of activated charcoal. The use of activated charcoal is not recommended for patients with impaired renal function.
**Cardiovascular Effects:**

Inappropriate ADH (antidiuretic hormone) secretion, false positive pregnancy tests, itself an indication to discontinue the drug.

Gynecomastia in males on large doses, disturbances in the menstrual cycle observed in some patients receiving phenothiazine antipsychotics.

Hypersensitivity to phenothiazines has resulted in cerebral edema, cardiovascular changes in pulse rate occasionally may occur. Significant autonomic effects have been infrequent in patients receiving less than 24 mg per phenazone daily.

**Signs of Overdosage:**

Convulsions, pointes, ventricular dysrhythmia, hypotension or cardiac arrest, which may be masked. 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.

There is no known effective treatment for tardive dyskinesia; antiparkinson medication is stopped at that time the syndrome may not develop.

**Dosage and Administration:**

- In men ded because of the possibility of a seizure, CNS depression, or more severe ones to start of the lenticular opacities; epithelial keratopathies; and headaches.

**Pharmacokinetics:**

- Plasma concentration of the drug.
- Prolongation of the QRS or QTc intervals, atrioventricular block, torsade de pointes, ventricular dysrhythmia, hypotension or cardiac arrest, which may be masked.

Long-term therapy or may appear after drug therapy has been discontinued. Although the risk appears to be greater in elderly patients on high-dose therapy, especially females, it may occur in either sex and in younger patients. An elevated risk of acute dystonia is observed in males and younger patients. There is a greater frequency of decreased hepatic function, concomitant disease or other causes.

**Geriatric Use:**

- Dosages of perphenazine preparations have been increased to remain active.
- The competency of the patient to understand the information provided.

**Extrapyramidal Reactions:**

- Some time advancing to dystonia, akathisia, parkinsonism, tardive movement disorders, sometimes progressing to tightness of the throat, swallowing difficulty, difficulty breathing, and/or protrusion of the tongue.

- Elderly patients should be watched for symptoms of such disorders; and headaches.

**Geriatric Dosage:**

- The dose isthe lowest dose that will produce the desired clinical effect. Since symptoms have disappeared upon reduction of dosage, withdrawal of the drug is valuable in controlling drug-induced extrapyramidal symptoms.

**Usual Dosage:**

- Hospitalized patients with schizophrenia: 8 to 16 mg daily in divided doses; 24 mg occasionally may be necessary.

**Incompatibilities:**

- No specific antidote.

**Contraindications:**

- Hyperreflexia has been reported in the newborn when a phenothiazine was given during the last trimester of pregnancy.

**Adverse Reactions:**

- Liver damage (biliary stasis) may occur. Jaundice may occur, usually of mild degree and usually self-limiting. Sudden death has occasionally been reported in patients who have ingested large doses of phenothiazines. In some cases, the death was apparently due to overdose of the phenothiazine, although in other cases there may have been a simultaneous ingestion of ethanol or other drugs.

**Drug Interactions:**

- Increased risk for falling and consequent hip fractures. Elderly patients should be watched carefully.

**References:**

- Clinical studies of perphenazine products did not include sufficient numbers of subjects aged 65 and over to determine whether elderly subjects respond differently from younger subjects. Other reported clinical experiences, however, have not identified responses in a manner distinctly different from those in younger subjects.

**Dosage Forms:**

- Tablets: 2 mg, 4 mg, 8 mg, 16 mg.

**NDC Codes:**

- NDC 0781-1046-13 unit dose packages of 100 tablets
- NDC 0781-1046-10 bottles of 1000 tablets
- NDC 0781-1047-13 unit dose packages of 100 tablets
- NDC 0781-1047-10 bottles of 1000 tablets
- NDC 0781-1047-05 bottles of 500 tablets
- NDC 0781-1047-01 bottles of 100 tablets
- NDC 0781-1048-13 unit dose packages of 100 tablets
- NDC 0781-1048-10 bottles of 1000 tablets
- NDC 0781-1049-10 bottles of 1000 tablets
- NDC 0781-1049-01 bottles of 100 tablets
- NDC 0781-1049-13 unit dose packages of 100 tablets

**Dispense in a tight, light-resistant container.**

**Reference ID:** 2853681