If signs and symptoms of tardive dyskinesia appear in a patient on antipsychotics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome. For further information about the description of tardive dyskinesia and its clinical detection, please refer to our clinical guidelines.

ADVERSE REACTIONS

Neuroleptic Malignant Syndrome (NMS): A potentially fatal syndrome commonly described as resemblingAKMalignant Hyperthermia Syndrome. The clinical manifestations are a triad of hyperthermia, tachycardia, and hyperglycemia. If these symptoms become too troublesome, they can usually be controlled by a reduction of dosage or drug withdrawal. However, if patients who have undergone chronic treatment, the syndrome may develop. Whether antipsychotic drugs differ in their potential to cause tardive dyskinesia is unknown.

Both the risk of developing the syndrome and the likelihood that it will be irreversible are believed to increase as the duration of treatment and the cumulative dose of antipsychotic drugs administered to the patient. Paranoid schizophrenia, the syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses.

There is no known treatment for established cases of tardive dyskinesia. Although the syndrome may remit, partially or completely, if antipsychotic drug treatment is withdrawn. Antipsychotic drug treatment itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome and thereby may prevent the development of the syndrome in susceptible patients. In patients who have received antipsychotic treatment as an antipsychotic. Although no causal relationship has been established, this possibility should be borne in mind.

Deep sleep, from which patients can be aroused, and coma have been reported, usually with overdosage. Antipsychotic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that prolactin-dependent, severe, non-neoplastic-dependent, in vitro; a factor of potential importance if the prescribing of these drugs is contemplated in a patient with a previously detected breast cancer. Although disturbances such as galactorrhea, amenorrhea, and impotence are well known, the mechanism underlying these effects has not been elucidated. However, the prostate of the male patient has been shown to demonstrate a response to phenothiazines in tissue culture experiments and in menopausal and asexual women have been demonstrated in patients treated with certain antipsychotics. As with all drugs which exert an anticholinergic effect, and/or cause mydriasis, prochlorperazine should be used with caution in patients with glaucoma because they may cause a paradoxical further lowering of blood pressure.

Because phenothiazines may produce false-positive phenylketonuria (PKU) test results.

There is evidence that phenothiazines are excreted in the breast milk of nursing mothers. It is recommended that women who breastfeed should avoid using prochlorperazine.

Non-teratogenic Effects: There have been reported instances of prolonged jaundice, extrapyramidal signs, hyperthermia, or hyperpyrexia in newborn infants whose mothers received prochlorperazine during pregnancy following delivery. These complications have varied in severity, while in some cases symptoms have been self-limited, in other cases neonates have required intensive care unit support and prolonged hospitalization.

The management of NMS should include 1) immediate discontinuation of antipsychotic drugs and other drugs that might be responsible for the NMS, 2) supportive management of fever, including initiating anticholinergic therapy and reversibly for patients on long-term antipsychotic therapy. A careful medical history should be obtained from the patient to help determine whether the condition is a result of NMS or another cause.

The presence of phenothiazines may interfere with thermoregulatory mechanisms, use with caution in persons with impaired cardiovascular regulation. In patients who are receiving such combined therapy should be considered. However, some patients may require treatment despite the presence of the syndrome. For further information about the description of tardive dyskinesia and its clinical detection, please refer to our clinical guidelines.

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Not all of the following adverse reactions have been observed with every phenothiazine derivative, but they have been reported with 1 or more and should be borne in mind when this class of drugs is administered: extrapyramidal symptoms (tremors, akathisia, dystonia, akathisia, dyskinesia, parkinsonism); some of which have lasted months and even years—particularly in elderly patients with previous brain damage; grand mal and petit mal convulsions, particularly in patients with EEG abnormalities or history of such disorders; altered cerebrospinal fluid proteins, cerebral edema; intensification and prolongation of the action of central nervous system depressants (opiates, analesics, antihistamines, barbiturates, alcohol), atropine, heat, organophosphorus insecticides; autonomic reactions (dryness of mouth, nasal congestion, headache, nausea, constipation, obstipation, adynamic ileus, exudatory disorders/impotence, priapism, atomic color, urinary retention, miosis and mydriasis); reactivation of psychotic processes, catatonic-like states; hypotension (sometimes total); cardiac arrest; blood dyscrasias (pancytopenia, thrombocytopenic purpura, leukopenia, agranulocytosis, eosinophilia, hemolytic anemia, aplastic anemia); liver damage (jaundice, bilary stasis); endocrine disturbances (hyperglycemia, hypoglycemia, glycosuria, lactation, galactorrhea, gynecomastia, menstrual irregularities, false-positive pregnancy tests); skin disorders (photosensitivity, itching, erythema, urticaria, eczema up to exfoliative dermatitis); other allergic reactions (asthma, laryngeal edema, angioneurotic edema, anaphylactic reactions); peripheral edema; reversed epinephrine effect; hyperpyrexia; mild fever after large I.M. doses; increased appetite; increased weight; a systemic lupus erythematosus-like syndrome; pigmentary retinopathy; with prolonged administration of substantial doses, skin pigmentation, epithelial keratopathy, and lenticonal and corneal deposits.

EXK changes—particularly nonspecific, usually reversible Q and T wave distortions have been observed in some patients receiving phenothiazine.

Although phenothiazines cause neither psychic nor physical dependence, sudden discontinuation in some patients receiving phenothiazine may result in the symptoms described above.

TREATMENT—It is important to determine other medications taken by the patient since multiple-dose therapy in common in overdose situations. Treatment is essentially symptomatic and supportive. Early gastric lavage is helpful. Keep patient under observation and maintain an open airway, since involvement of the extrapyramidal mechanism may produce dysphagia and respiratory difficulty in severe overdose. Do not attempt to induce emesis because a dystonic reaction of the head or neck may develop that could result in aspiration of vomitus. Extrapyramidal symptoms may be treated with antipsychotics, barbiturates or Benadryl. See prescribing information for these products. Care should be taken to avoid increasing respiratory depression.

If administration of a stimulant is desirable, amphetamine, dextroamphetamine or caffeine with sodium benzoate is recommended.

Stimulants that may cause convulsions (e.g., phencyclidine or pentylentetrazol) should be avoided. If hypotension occurs, the standard measures for managing circulatory shock should be initiated. If it is desirable to administer a vasopressor, Levoephed and Neo-Synephrine are most suitable. Other pressor agents, including epinephrine, are not recommended because phenothiazine derivatives may increase the usual elevating action of these agents and cause further lowering of blood pressure.

Limited experience indicates that phenothiazines are not dialyzable.

Dosage and Administration—Adults

For children’s dosage and administration, see below.) 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 neuro muscular 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.

1. To Control Severe Nausea and Vomiting: Adjust dosage to the response of the individual. Begin with the lowest recommended dosage.

Oral Dosage—Tablets: Usual one 5mg or 10mg tablet 3 or 4 times daily. Usually elevating action of these agents and cause further lowering of blood pressure.

In more severe disturbances, optimum dosage is usually 100 to 150mg daily.

DOSAGE AND ADMINISTRATION—Children

Do not use in pediatric surgery.

Children seem more prone to develop extrapyramidal reactions, even on moderate doses. Therefore, use lowest effective dosage. Tell parents not to exceed prescribed dosage, since the possibility for adverse reactions increases as dosage rises. Occasionally the patient may react to the drug with signs of restlessness and excitement; if this occurs, do not administer additional doses. Take particular precaution in administering the drug to children with acute illnesses or dehydration (see under Dystonias).

1. Severe Nausea and Vomiting in Children: Prochlorperazine should not be used in pediatric patients under 20 pounds or 2 years of age. It should not be used in conditions for which children’s dosages have not been established. Dosage and frequency of administration should be adjusted according to the severity of the symptoms and the response of the patient. The duration of activity following intramuscular administration may last up to 12 hours. Subsequent doses may be given by the same route if necessary.

Oral Dosage: More than 1 day’s therapy is seldom necessary.

<table>
<thead>
<tr>
<th>Weight</th>
<th>Usual Dosage</th>
<th>Not to Exceed</th>
</tr>
</thead>
<tbody>
<tr>
<td>under 20 lbs not recommended</td>
<td>2½ mg 1 or 2 times a day</td>
<td>10 mg per day</td>
</tr>
<tr>
<td>20 to 29 lbs</td>
<td>1½ mg 1 or 2 times a day</td>
<td>15 mg per day</td>
</tr>
<tr>
<td>30 to 49 lbs</td>
<td>1½ mg 1 or 2 times a day</td>
<td>20 mg per day</td>
</tr>
<tr>
<td>50 to 85 lbs</td>
<td>2½ mg 1 or 2 times a day</td>
<td>30 mg per day</td>
</tr>
</tbody>
</table>

HOW SUPPLIED

Prochlorperazine Maleate Tablets USP are available in the following strengths and package sizes:

5mg Charterhouse, round, film coated tablets debossed with ‘TL 115’ scored on one side and plain on the other side.

Bottles of 100 NDC 59746-113-10
Bottles of 1000 NDC 59746-113-10

Storage

Store at 20 - 25°C (68 - 77°F) [See USP Controlled Room Temperature]. Protect from light. Dispense in a light-tight, resistant container.

* diphenhydramine bitartrate, Abbott Laboratories.
** phenytoin, Parke Davis.
§ metrizamide, Sanofi Pharmaceuticals.
¶ diphenhydramine hydrochloride, Parke Davis.

Manufactured by:

Jubilant Cadista Pharmaceuticals Inc.
Salisbury, MD 21801, USA

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