

**DRUGS-ABOUT.COM****PHYSICIAN'S PRESCRIBING INFORMATION****TAROCTYL**  
**TABLETS & INJECTIONS****Composition:**

Tarocetyl contains chlorpromazine and is present in oral and injectable forms as the hydrochloride salt.

**Therapeutic class:**

Antipsychotic, Antiemetic

**Dosage form:**

Tablets: 25 mg, 100 mg  
I.V. injections: 50 mg/2ml  
I.M. injections: 25 mg/5ml

**Mechanism of action:**

Chlorpromazine is a dimethylamine derivative of phenothiazine. The precise mechanism whereby the therapeutic effects of chlorpromazine are produced is not known. The principal pharmacological actions are psychotropic. It also exerts sedative and antiemetic activity. Chlorpromazine has actions at all levels of the central nervous system, primarily at subcortical levels, as well as on multiple organ systems. Chlorpromazine has strong antiadrenergic and weaker peripheral anticholinergic activity; ganglionic blocking action relatively slight. It also possesses slight antihistaminic and antiserotonin activity.

**Pharmacokinetics:****Absorption:**

Oral- erratic and variable. Peak plasma levels are seen 2 to 4 hours following oral administration.

I.M.- 4-10 times more active than oral doses

**Distribution:**

Widely distributed in tissues. CNS concentrations exceed those in the plasma. Highly bound to plasma proteins (90% or more). Stored and accumulate in the brain, lungs and other well perfused tissues and may be found in the urine for up to 6 months after the last dose.

**Onset of action:**

Antipsychotic effect: Gradual (up to several weeks) and variable between patients.

Time to peak effect: Antipsychotic effect: Approximately 4 to 7 days to achieve steady - state plasma concentrations; peak therapeutic effects may take from 6 weeks to 6 months.

**Metabolism:**

Extensive biotransformation occurs in the liver.

Since plasma concentrations of this drug are highly variable from patient to patient, plasma monitoring may be useful to determining therapeutic response and help decrease the incidence of toxicity since plasma levels are relatively stable in each individual.

**Indications:**

- For short term treatment of severe anxiety and relief of restlessness.
- For the management of manifestation of psychotic disorders especially in mania.
- To control nausea and vomiting.
- Hyperexcitable behavior.
- For acute intermittent porphyria.
- As an adjunct in the treatment of tetanus.
- To control intractable hiccups.
- Hyperkinesia in children.

**Contraindications:**

Except under special circumstances, this medicine should not be used when the following medical problems exist:

- Cardiovascular disease.
- CNS depression and when taking large amounts of central nervous system depressants (alcohol, barbiturates, narcotics, etc.) (see precautions).
- Comatose states (may be exacerbated).
- Reye's syndrome - The extrapyramidal symptoms which can occur secondary to chlorpromazine may be confused with the CNS signs of an undiagnosed primary disease responsible for the vomiting, e.g. Reye's syndrome or other encephalopathy. The use of chlorpromazine and other potential hepatotoxins should be avoided in children and adolescents whose signs and symptoms suggest Reye's syndrome.

Risk and benefit should be considered when the following medical problems exist:

- Alcoholism
- Hepatic function impairment.
- Hypersensitivity- Cross sensitivity between phenothiazines may occur.
- Patients with bone marrow depression and blood dyscrasias.

**Warnings:**

**Tardive dyskinesia:** A syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may develop in patients treated with neuroleptic (antipsychotic) drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of neuroleptic treatment, which patients are likely to develop the syndrome. Whether neuroleptic drug products differ in their potential to cause tardive dyskinesia is unknown.

Both the risk of developing the syndrome and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of neuroleptic drugs administered to the patient increase. However, 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 neuroleptic treatment is withdrawn. Neuroleptic treatment itself, however, may suppress (or partially suppress) the signs and symptoms of the syndrome

and thereby may possibly mask the underlying disease process. The effect that symptomatic suppression has upon the long term course of the syndrome is unknown.

Given these considerations, neuroleptic should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic neuroleptic treatment should generally be reserved for patients who suffer from a chronic illness that: 1. is known to respond to neuroleptic drugs, and, 2. for whom alternative, equally effective, but potentially less harmful treatments are not available or appropriate. In patients who do require chronic treatment, the smallest dose and the shortest duration of treatment producing a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically.

If signs and symptoms of tardive dyskinesia appear in a patient on neuroleptics, drug discontinuation should be considered. However, some patients may require treatment despite the presence of the syndrome.

**Neuroleptic Malignant Syndrome (NMS):** A potentially fatal symptom complex sometimes referred to as NMS has been reported in association with antipsychotic drugs. Clinical manifestation of NMS are hyperpyrexia, muscle 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). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever and primary 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. 3) Treatment of any concomitant serious medical problems for which specific treatments are available.

There is no general agreement about specific pharmacological treatment regimens for uncomplicated NMS.

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.

**Hypersensitivity to sodium bisulfite:** Tarocetyl ampoules contain sodium bisulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

**CNS effects:** Chlorpromazine may impair mental and/or physical abilities, especially during the first few days of therapy. Therefore caution patients about activities requiring alertness (e.g. operating vehicles or machinery).

**Antiemetic effects:** Chlorpromazine has antiemetic effect that can obscure signs of toxicity of other drugs, or mask symptoms of disease (e.g. brain tumor, intestinal obstruction, Reye's syndrome). Because these drugs can suppress the cough reflex, aspiration of vomits is possible.

**Pregnancy:**

Safety for the use of chlorpromazine during pregnancy has not been established. Therefore, it is not recommended that the drug be given to pregnant patients except when, in the judgment of the physician, it is essential. The potential benefits should clearly outweigh possible hazards. There are reported instances of prolonged jaundice, extrapyramidal signs, hyperreflexia or hyporeflexia in newborn infants whose mothers received phenothiazines.

Reproductive studies in rodents have demonstrated potential for embryotoxicity, increased neonatal mortality and nursing transfer of the drug. Tests in the offspring of the drug-treated rodents demonstrate decrease performance. The possibility of permanent neurological damage cannot be excluded.

**Lactation:**

The use of chlorpromazine in nursing mothers is not recommended. There is evidence that chlorpromazine is excreted in the breast milk of nursing mothers.

**Adverse reactions:**

**Note:** Some adverse effects of chlorpromazine may be more likely to occur, or occur with greater intensity, in patients with special medical problems, e.g. patient with mitral insufficiency or pheochromocytoma have experienced severe hypotension following recommended doses.

**Sudden death:** Death has occasionally been reported, especially in patients with previous brain damage or seizures. In some cases, the cause appeared to be cardiac arrest or asphyxia due to the failure of the cough reflex.

**Hepatic:** Jaundice - Overall incidence has been low, regardless of identification or dosage. Most cases occurs between the second and fourth weeks of therapy and is regarded as hypersensitivity reaction.

If fever with grippelike symptoms occurs, appropriate liver studies should be conducted. If tests indicate an abnormality, stop treatment.

Liver function tests in jaundice induced by the drug may mimic extrahepatic obstruction; withhold exploratory laparotomy until extrahepatic obstruction is confirmed.

**Hematologic:** Eosinophilia; leukopenia; leucocytosis; anemia; tendency toward lymphomonocytosis; thrombocytopenic purpura; pancytopenia.

**Agranulocytosis:** Most cases have occurred between weeks 4 and 10 of therapy. Watch for the sudden appearance of soreness of the mouth, gums or throat or other signs of infection. If white cell count and differential show significant cellular depression, discontinue use. A slight lowered white count alone is not an

indication to discontinue the drug.

**Cardiovascular:** Hypotension; postural hypotension; hypertension; tachycardia (especially with rapid increase in dosage); bradycardia; cardiac arrest; circulatory collapse; syncope; lightheadedness; faintness; dizziness. The hypotensive effect may occasionally produce a shock-like condition.

To minimize hypotension after injection, keep patient lying down and observe for at least 1/2 hour. To control hypotension, place patient in head-low position with legs raised.

If a vasoconstrictor is required, norepinephrine and phenylephrine are the most suitable. Other pressor agents, including epinephrine, should not be used as they may cause a paradoxical further lowering of blood pressure. EKG changes, particularly non-specific, usually reversible Q and T wave distortions have been observed in some patients receiving phenothiazine tranquilizers, including chlorpromazine.

**Extrapyramidal:** These are usually dose-related and take three forms: Pseudoparkinsonism (4% to 40%), akathisia (7% to 20%); dystonias (2% to 50%) (see warnings: tardive dyskinesia).

Pseudoparkinsonism- Symptoms may include: mask-like face, drooling, tremors, pill-rolling motion, cogwheel rigidity and shuffling gait. In most cases these symptoms are readily controlled when an anti-parkinsonism agent is administered concomitantly.

Akathisia- Symptoms may include agitation or jitteriness and sometimes insomnia.

These symptoms often disappear spontaneously. At times these symptoms may be similar to the original neurotic or psychotic symptoms. Dosage should not be increased until these side effects have subsided.

Dystonias- Symptoms may include spasm of the neck muscles, sometimes progressing to acute, reversible torticollis; extensor rigidity of back muscles sometimes progressing to opisthotonos; carpedal spasm, trismus, swallowing difficulty, oculogyric crisis and protrusion of the tongue.

These usually subside within a few hours, and almost always within 24 to 48 hours after the drug has been discontinued.

Management of extrapyramidal symptoms includes use of barbiturate, antipsychotic dosage reduction and anticholinergic-type antiparkinson agents. Prophylactic anticholinergic medication is controversial. Parenteral diphenhydramine, 50 mg (2mg/kg, to maximum of 50 mg for children), or parenteral benztropine, 2 mg, will ameliorate the acute dystonic reaction within 2 to 5 minutes when given IV or within 30 to 60 minutes when given IM. Employ supportive measures such as maintaining a clear airway and adequate hydration. Anticholinergics are often ineffective for akathisia; benzodiazepines, propranolol and clonidine have been used.

**Adverse behavioral effects:** Exacerbation of psychotic symptoms including hallucinations; catatonic like states; lethargy; restlessness; hyperactivity; agitation; nocturnal confusion; toxic confusional states; bizarre dreams; depression; euphoria; excitement; paranoid reactions.

**Other CNS effects:** Cerebral edema; headache; weakness; tremor; staggering gait; twitching tension; akinesia; ataxia; fatigue; slurring; abnormal cerebrospinal fluid proteins; vertigo; drowsiness (80 % usually lasts 1 week), NMS (see warnings).

Convulsive seizures (Petit Mal and Grand Mal) have been reported, particularly in patients with EEG abnormalities or history of such disorders.

**Dermatologic/allergic:** urticaria (5%), maculopapular hypersensitivity reactions, pruritus. Photosensitivity may occur. Avoid undue exposure to sun. More severe reactions, including exfoliative dermatitis, have been reported occasionally.

In addition, asthma, laryngeal edema, angioneurotic edema and anaphylactoid reactions have been reported.

**Autonomic:** Dry mouth; nasal congestion; nausea; vomiting; paresthesia; anorexia, pallor, flushed face.

**Endocrine disorders:** Lactation and moderate breast engorgement may occur in females on large doses. If persistent, lower dosage or withdraw drug. False positive pregnancy tests have been reported, but are less likely to occur when a serum test is used. Amenorrhea and gynecostasia have also been reported.

Hyperglycemia, hypoglycemia and glycosuria have been reported.

**Heatstroke/hyperpyrexia:** Induced by neuroleptics has occurred.

**Ocular:** Glaucoma, photophobia, blurred vision, miosis, mydriasis, ptosis.

**Respiratory:** Laringospasm, bronchospasm, increased depth of respiration, dyspnea.

**Other adverse reactions reported included:** Constipation, adynamic ileus, urinary retention, priapism, atonic colon, ejaculatory disorders/impotence.

Mild fever may occur after large I.M. doses. Increases in appetite and weight sometimes occur. Peripheral edema and a systemic lupus erythematosus-like syndrome have been reported.

**Special considerations in long-term therapy:** Skin pigmentation and ocular changes have occurred in some patients taking substantial doses of chlorpromazine for prolonged periods.

Skin pigmentation - Rare instances of skin pigmentation have been observed in hospitalized mental patients, primarily females who have received the drug usually for 3 years or more in dosages ranging from 500mg to 1500mg daily.

The pigmentary changes, restricted to exposed areas of the body, range from an almost imperceptible darkening of the skin to a slate gray color, sometimes with a violet hue. Histological examination reveals a pigment, chiefly in the dermis, which is probably a melanin-like complex. The pigmentation may fade following discontinuance of the drug.

Ocular changes- Ocular changes have occurred more frequently than skin pigmentation and have been observed both pigmented and nonpigmented patients receiving chlorpromazine usually for 2 years or more in dosages of 300mg daily and higher. Eye changes are characterized by deposition of fine particulate matter in the lens and cornea. In more advanced cases, star-shaped opacities have also been observed in the anterior portion of the lens. The nature of the eye deposits has not yet been determined.

A small number of patients with more severe ocular changes have had some visual impairment. In addition to these corneal and lenticular changes, epithelial keratopathy and pigmentary retinopathy have been reported. Reports suggest that the eye

lesions may regress after withdrawal of the drug. Since the occurrence of eye changes seems to be related to dosage levels and/or duration of therapy, it is suggested that long-term patients on moderate to high dosage levels have periodic ocular examinations.

**Etiology-** The etiology of both of these reactions is not clear, but exposure to light, along with dosage/duration of therapy, appears to be the most significant factor. If either of these reactions is observed, the physician should weigh the benefits of continued therapy against the possible risks and, on the merits of the individual case, determine whether or not to continue present therapy, lower the dosage, or withdraw the drug.

#### **Drug interactions:**

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance: **Alcohol or other CNS depression producing medications** - concurrent use with phenothiazines may result in increased CNS and respiratory depression and increase hypotensive effects. Dosage reductions of either drug may be necessary during concurrent use or when sequence of use enhances CNS effects. **Amantadine or anticholinergics or antihistamines or anticholinergic or other medications with anticholinergic action** - concurrent use with phenothiazines may intensify anticholinergic side effects, especially confusion, hallucinations and nightmares, because of the phenothiazines secondary anticholinergic effects; medications with anticholinergic effects may potentiate the hyperpyretic effect of phenothiazines, especially when environmental temperatures are high, by preventing sweating as a cooling mechanism; this effect could lead to heat stroke; also, patients should be advised to report occurrence of gastrointestinal problems since paralytic ileus may occur with concurrent therapy.

**Antacids, aluminum- or magnesium-containing or absorbent antidiarrheals** - concurrent use of these medications with phenothiazines may inhibit the absorption of orally administered phenothiazines, especially chlorpromazine; simultaneous use should be avoided.

**Anticonvulsants, including Barbiturates** - phenothiazines may lower the seizure threshold; dosage adjustment of anticonvulsant medications may be necessary. Phenothiazines may inhibit phenytoin metabolism, leading to phenytoin toxicity.

**Tricyclic antidepressants or Maprotiline or MAO inhibitors, furazolidone, procarbazine and selegiline** - concurrent use may prolong and intensify the sedative and anticholinergic effects of either these medications or phenothiazines. Phenothiazines may increase plasma concentrations of cyclic antidepressants by inhibiting metabolism; conversely, cyclic antidepressants may inhibit phenothiazine metabolism. The risk of NMS (neuroleptic malignant syndrome) may be increased.

**Antithyroid agents** - concurrent use with phenothiazines may increase the risk of agranulocytosis.

**Appetite suppressants** - concurrent use with phenothiazines may antagonize the anorectic effect of appetite suppressants, with the exception of fenfluramine and phentermine.

**Beta-adrenergic blocking agents** - concurrent use of beta-blockers, possibly including ophthalmics, with phenothiazines may result in an increased plasma concentration of each medication because of inhibition of metabolism; this may result in additive hypotensive effects, irreversible retinopathy, cardiac arrhythmias, and tardive dyskinesia.

**Bromocriptine** - concurrent use may increase serum prolactin concentrations and interfere with effects of bromocriptine; dosage adjustments may be necessary.

**Epinephrine** - The use of epinephrine to treat phenothiazine-induced hypotension should be avoided because the alpha adrenergic effects of epinephrine may be blocked, resulting in beta stimulation only and causing severe hypotension and tachycardia.

**Lithium** - concurrent use with chlorpromazine and possibly other phenothiazines may reduce gastrointestinal absorption of the phenothiazine, thereby decreasing its serum concentrations by as much as 40%; concurrent use may increase the rate of renal excretion of lithium; extrapyramidal symptoms may be increased; also, nausea and vomiting, early indications of lithium toxicity may be masked by the antiemetic effect of some phenothiazines.

**Metrizamide** - concurrent use with phenothiazines may lower the seizure threshold; phenothiazines should be discontinued at least 48 hours before, and not resumed for at least 24 hours following myelography.

**Opioid (narcotic) analgesics** - in addition to increased CNS and respiratory depression, concurrent use with phenothiazines increases orthostatic hypotension and increases the risk of severe constipation, which may lead to paralytic ileus and/or urinary retention.

The antihypertensive effect of **guanethidine and related compounds** may be counteracted when used concurrently with phenothiazines.

**Thiazide diuretics** may accentuate the orthostatic hypotension that may occur.

**Charcoal** can prevent the absorption of phenothiazines. Depending on the clinical situation, this will reduce the effectiveness or toxicity of the phenothiazine.

#### **Precautions:**

- Given the likelihood that some patients exposed chronically to neuroleptic 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. The decision to inform patients and/or their guardians must obviously take into account the clinical circumstances and the competency of the patient to understand the information provided.
- Because of its CNS depressant effect, Taroclyl should be used with caution in patients with chronic respiratory disorders such as severe asthma, emphysema and acute respiratory infections, particularly in children.
- Chlorpromazine prolongs and intensifies the action of CNS depressants such as anesthetics, barbiturates and narcotics. When chlorpromazine is administered concomitantly, about

0.25 to 0.5 the usual dosage of such agents is required. When chlorpromazine is not being administered to reduce requirements of CNS depressants, it is best to stop such depressants before starting treatment. These agents may subsequently be reinstated at low doses and increased as needed.

**Note** - chlorpromazine does not intensify the anticonvulsant action of barbiturates.

Therefore, dosage of anticonvulsants, including barbiturates, should not be reduced if it is started. Instead, start chlorpromazine low doses and increase as needed.

- Use with caution in persons who will be exposed to organophosphorus insecticides, and in persons receiving atropine or related drugs.
- Neuroleptic drugs elevate prolactin levels; the elevation persists during chronic administration. Tissue culture experiments indicate that approximately 1/3 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 previously detected 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 has been found in rodents after chronic administration of neuroleptic drugs. Neither clinical nor epidemiological 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.
- The presence of phenothiazines may produce false-positive phenylketonuria (PKU) test results.
- Since phenothiazines may lower the seizure threshold, the drugs should be used with caution in patients with history of seizures and in those receiving anticonvulsants agents. Adequate anticonvulsants therapy should be maintained during administration of phenothiazines.
- Phenothiazines should be used with caution in geriatric or debilitated patients, in patients with renal disease, and in patients with prostatic hypertrophy.
- Because phenothiazines depress the hypothalamic mechanism for regulation of body temperature, the drugs should also be administered with caution to patients exposed to extreme heat or cold; patients receiving phenothiazines should be advised that they are likely to have an increased vulnerability when exposed to temperature extremes, possibly resulting in hyperthermia or hypothermia.
- Chlorpromazine should be used with caution in patients with glaucoma.
- Long-term therapy: to lessen the likelihood of adverse reactions related to cumulative drug effect, patients with a history of long-term therapy with chlorpromazine and/or other neuroleptics should be evaluated periodically to decide whether the maintenance dosage could be lowered or drug therapy discontinued.
- Abrupt withdrawal: Like other phenothiazines, chlorpromazine is not known to cause psychic dependence and does not produce tolerance or addiction. There may be, however, following abrupt withdrawal of high-dose therapy, some symptoms resembling those of physical dependence such as gastritis, nausea and vomiting, dizziness and tremulousness. These symptoms can usually be avoided or reduced by gradual reduction of the dosage or by continuing concomitant anti-parkinsonism agents for several weeks after chlorpromazine is withdrawn.

#### **Dosage and Administration:**

Oral administration is the preferred route especially in long-term treatment for chronic conditions.

Oral administration can successfully substitute for the parenteral route, or be used to complete parenteral course of treatment in order to avoid a sudden interruption of such a course.

Intramuscular injections should be sited deeply into the upper-outer quadrant of the gluteal muscle.

Intravenous injections: The necessity for IV injections seldomly arises. The 2 ml ampoule should never be administered undiluted. It should be diluted to 1 mg/ml in physiological solution and administered as a drip infusion, at a rate of 1 mg/minute.

Adjust dosage to individual and the severity of his condition, recognizing that the milligram for milligram potency relationship among all dosage forms has not been precisely established clinically. It is important to increase dosage until symptoms are controlled. Dosage should be increased more gradually in debilitated or emaciated patients. In continued therapy, gradually reduce dosage to the lowest effective maintenance level, after symptoms have been controlled for a reasonable period.

Elderly patients: In general, dosage 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.

Chlorpromazine should generally not be used in children under 6 months of age except where potentially lifesaving. It should not be used in conditions for which specific children's dosage have not been established.

#### **Parenteral dosage form:**

##### **Usual adult dose:**

**Psychotic disorders (severe):** I.M.: 25 to 50 mg, the dose being repeated in one hour if needed, and every three to twelve hours thereafter as needed and tolerated. The dosage may be gradually increased over several days as needed and tolerated.

**Nausea and vomiting:** I.M.: 25 mg in a single dose, the dosage being increased to 25 to 50 mg every three to four hours as needed and tolerated until vomiting stops.

**Nausea and vomiting during surgery:** I.M.: 12.5 mg in a single dose, the dose being repeated in thirty minutes as needed and tolerated.

**I.V. infusion:** Up to 25 mg, diluted to a concentration of at least 1 mg per ml of 0.9% sodium chloride injection, administered at a rate of no more than 2 mg every 2 minutes.

**Anxiety, presurgical:** I.M.: 12.5 to 25 mg one or two hours before surgery.

**Hiccups:** I.M.: 25 to 50 mg three or four times a day.

**I.V. infusion:** 25 to 50 mg, diluted in 500 to 1000 ml sodium chloride injections, administered slowly at a rate of 1 mg per minute.

**Porphyria:** I.M.: 25 mg every six or eight hours until patient can take oral therapy.

**Tetanus:** I.M.: 25 to 50 mg three or four times a day, the dosage being increased gradually as needed and tolerated.

**I.V. infusion:** 25 to 50 mg diluted to a concentration of at least 1 mg per ml with sodium chloride injection, administered at a rate of 1 mg per minute.

**Usual adult prescribing limits:** Up to 1 gram a day.

#### **Usual pediatric dose:**

**Psychotic disorders or nausea and vomiting:** Children up to 6 months of age: Dosage has not been established.

Children 6 months of age and over: I.M.: 550 mcg per kg of body weight or 15 mg per square meter body surface every six to eight hours as needed.

**Nausea and vomiting during surgery:** I.M.: 275 mcg per kg of body weight, the dosage being repeated in thirty minutes as needed and tolerated.

**I.V. infusion:** 275 mcg per kg of body weight, diluted to a concentration of at least 1 mg per ml with 0.9% sodium chloride injection, administered at a rate of no more than 1 mg every 2 minutes.

**Anxiety, presurgical:** I.M.: 550 mcg per kg of body weight, one to two hours before surgery.

**Tetanus:** I.M.: 550 mcg per kg of body weight, every six to eight hours.

**I.V. infusion:** 550 mcg per kg of body weight diluted to a concentration of at least 1 mg per ml with 0.9% sodium chloride injection, administered at a rate of 1 mg per 2 minutes.

**Usual pediatric prescribing limits:** Children 6 months to 5 years of age (up to 23 kg) should receive no more than 40 mg a day. Children 5 years to 12 years of age (23 to 46kg) should receive no more than 75 mg a day except of unmanageable cases.

#### **Oral dosage form:**

##### **Usual adult dose:**

**Psychotic disorders:** 10 to 25 mg, two to four times a day, the dosage being increased by 20 to 50 mg a day every three to four days as needed and tolerated.

**Nausea and vomiting:** 10 to 25 mg every four hours, the dosage being increased as needed and tolerated.

**Anxiety, presurgical:** 25 to 50 mg two or three hours before surgery.

**Hiccups or Porphyria:** 25 to 50 mg three or four times a day.

**Usual adult prescribing limits:** Up to 1 gram a day.

#### **Usual pediatric dose:**

##### **Psychotic disorders or nausea and vomiting:**

Children up to 6 months of age: Dosage has not been established. Children 6 months of age and over: 550 mcg per kg of body weight or 15 mg per square meter body surface every four to six hours, the dosage being adjusted as needed and tolerated.

**Anxiety, presurgical:** 550 mcg per kg of body weight or 15 mg per square meter body surface two to three hours before surgery.

#### **Overdosage:**

##### **Symptoms:**

Primarily symptoms of CNS depression to the point of somnolence or coma.

Hypotension and extrapyramidal symptoms.

Other possible manifestation include agitation and restlessness, convulsions, fever, autonomic reactions such as dry mouth and ileus, ECG changes and cardiac arrhythmias.

##### **Treatment:**

Includes usual supportive measures. Emetics are unlikely to be of value due to the antiemetic effects of this drug, and induction of emesis may result in a dystonic reaction of the head or neck that could result in aspiration of vomits.

Extrapyramidal symptoms may be treated with antiparkinson drugs, barbiturates or diphenhydramine.

If hypotension occurs, initiate the standard measures for managing circulatory shock, including volume replacement. If a vasoconstrictor is desired, use norepinephrine or phenylephrine. Do not administer epinephrine.

Control convulsions or hyperactivity with pentobarbital or diazepam.

#### **Diagnostic interference:**

- False-positive pregnancy tests, less likely to occur when a serum test is used.
- May discolor the urine pink to red brown.

#### **Storage conditions:**

Store in a cool (between 15 and 30°C) dark place. If after the course of treatment, some of the drug is left destroy it.

#### **Presentation:**

Tablets 25 mg and 100 mg in 50 tablets boxes.

IV injections 50 mg/2 ml in 50 ampoules boxes.

IM injections 25 mg/5 ml in 50 ampoules boxes.

#### **Manufacturer:**

Taro Pharmaceutical Industries Ltd.,  
P.O.B. 10347, Haifa Bay 26110, Israel.

#### **License numbers:**

1488.24450; 1487.24451; 1463.24441; 1486.24443