PRODUCT MONOGRAPH

STEMETIL®

Prochlorperazine mesylate injection

10 mg/2 mL prochlorperazine as prochlorperazine mesylate

Prochlorperazine Suppositories

10 mg

Antipsychotic - Antiemetic

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PRODUCT MONOGRAPH

NAME OF DRUG

Stemetil

Prochlorperazine mesylate injection

Prochlorperazine Suppositories

THERAPEUTIC CLASSIFICATION

Antipsychotic - Antiemetic

ACTION

Stemetil (prochlorperazine) is a piperazine phenothiazine derivative with antipsychotic, antiemetic and weak sedative activity.

Stemetil has actions similar to those of other phenothiazine derivatives but appears to be less sedating and to have a weak propensity for causing hypotension or potentiating the effects of CNS depressants and anesthetics. However, it produces a high incidence of extrapyramidal reactions.

INDICATIONS

Stemetil (prochlorperazine) is indicated in the management of manifestations of psychotic disorders such as agitation, confusion, delusion, tension and anxiety.

It is also effective in controlling nausea and vomiting due to stimulation of the chemoreceptor trigger zone.

In selected patients, Stemetil may be of value for the relief of excessive anxiety, accompanied by severe tension and agitation, associated with psychoneurotic or somatic conditions.

CONTRAINDICATIONS

Stemetil (prochlorperazine) should not be administered in the presence of circulatory collapse, altered states of consciousness or comatose states, particularly when these are due to intoxication with central depressant drugs (alcohol, hypnotics, narcotics, etc.). It is contraindicated in severely depressed patients, in the presence of blood dyscrasias, liver disease, renal insufficiency, pheochromocytoma, or in patients with severe cardiovascular disorders or a history of hypersensitivity to phenothiazine derivatives.

As with other phenothiazines, Stemetil is contraindicated in patients with suspected or established subcortical brain damage, with or without hypothalamic damage, since a hyperthermic reaction with temperatures above 40°C may occur, sometimes not until 14 to 16 hours after drug administration.

Phenothiazine compounds should not be used in patients receiving large doses of hypnotics, due to the possibility of potentiation.

Stemetil is contraindicated in children undergoing surgery.

WARNINGS

The antiemetic action of Stemetil (prochlorperazine) may mask the signs and symptoms of overdosage of other drugs and may obscure the diagnosis and treatment of other conditions such as brain tumor or intestinal obstruction. Therefore the etiology of nausea and vomiting should be established before using the drug.

The use of this drug may impair the mental and physical abilities required for the performance of potentially hazardous tasks, such as driving a car or operating machinery. Potentiation of the effects of alcohol may also occur.

As with other neuroleptics, very rare cases of QT interval prolongation have been reported with Stemetil. Neuroleptic phenothiazines may potentiate QT interval prolongation, which increases the risk of onset of serious ventricular arrhythmias of the torsade de pointes type, which is potentially fatal (sudden death). QT prolongation is exacerbated, in particular, in the presence of bradycardia, hypokalemia, and congenital or acquired (i.e., drug induced) QT prolongation. If the clinical situation permits, medical and laboratory evaluations should be performed to rule out possible risk factors before initiating treatment with a neuroleptic agent and as deemed necessary during treatment (See also PRECAUTIONS and ADVERSE REACTIONS).

Tardive Dyskinesia: As with all antipsychotic agents, tardive dyskinesia may appear in some patients on long-term therapy or after drug discontinuation. The syndrome is mainly characterized by rhythmical involuntary movements of the tongue, face, mouth or jaw. The manifestations may be permanent in some patients. The syndrome may be masked when treatment is reinstituted, when the dosage is increased or when a switch is made to a different antipsychotic drug. Stemetil should be prescribed in a manner that is most likely to minimize the risk of tardive dyskinesia. The lowest effective dose and the shortest duration of treatment should be used, and treatment should be discontinued at the earliest opportunity, or if a satisfactory response cannot be obtained. If the signs and symptoms of tardive dyskinesia appear during treatment, discontinuation of Stemetil should be considered.

Neuroleptic Malignant Syndrome: Neuroleptic malignant syndrome (NMS) may occur in patients receiving antipsychotic drugs. NMS is characterized by hyperthermia, muscle rigidity, altered consciousness, and signs of autonomic instability including irregular blood pressure, tachycardia, cardiac arrhythmias and diaphoresis. Additional signs may include elevated serum creatine kinase, myoglobinuria (rhabdomyolysis), acute renal failure and leukocytosis. Hyperthermia is often an early sign of this syndrome. Antipsychotic treatment should be withdrawn immediately and appropriate supportive therapy and careful monitoring instituted.

Use in pregnancy: Safety for the use of Stemetil (prochlorperazine) during pregnancy has not been established. Therefore, it is recommended that the drug be given to pregnant patients only when, in the judgement of the physician, the potential benefit to the patient outweighs the possible risk to the fetus.

Use in children: The drug should not be used in children under 2 years unless potentially life-saving.

The extrapyramidal symptoms which can occur secondary to Stemetil may be confused with the central nervous system signs of an undiagnosed primary disease responsible for the vomiting, e.g. Reye's syndrome or other encephalopathy. The use of prochlorperazine should be avoided in children and adolescents whose signs and symptoms suggest Reye's syndrome.

PRECAUTIONS

The increased incidence of seizures, which occasionally occur in epileptics started on antipsychotic medication, may be controlled by increasing the dosage of their anticonvulsant. Patients with a familial history of seizures or febrile convulsions are more likely to develop seizures than those who have no such history.

Phenothiazines may increase the effects of general anesthetics, opiates, barbiturates, and other CNS depressants and the doses of these drugs should be reduced if administered concomitantly with Stemetil (prochlorperazine).

On long-term therapy, particularly during the first two or three months, it is advisable to perform periodic liver function tests and blood counts as cholestatic jaundice and blood dyscrasias may occur, necessitating discontinuation of treatment. Renal function should be monitored and, if BUN (blood urea nitrogen) becomes abnormal, treatment should be discontinued.

To lessen the likelihood of adverse reactions related to drug accumulation, patients on long-term therapy, particularly on high doses, should be evaluated periodically to decide whether the maintenance dosage could be lowered or drug therapy discontinued.

Because of its anticholinergic action, Stemetil should be used with great caution in patients with glaucoma or prostatic hypertrophy.

The effects of anticholinergic drugs may be potentiated by prochlorperazine. Paralytic ileus, even resulting in death, may occur, especially in the elderly. Caution should be observed if constipation develops.

Retinal changes, lenticular and corneal deposits and abnormal skin pigmentation have been observed with other phenothiazines and may occur after prolonged therapy. The possibility of persistent tardive dyskinesia should also be borne in mind when patients are under long-term treatment.

Patients receiving prochlorperazine should be cautioned against exposure to extreme heat or organophosphorous insecticides.

False positive or negative pregnancy tests have occurred in patients receiving phenothiazine therapy.

Hypotension and electrocardiographic changes, particularly non-specific and usually reversible Q and T wave distortions, have been associated with the administration of phenothiazines. Therefore, prochlorperazine should be used with caution in patients with compensated cardiovascular and cerebrovascular disorders.

Neuroleptic phenothiazines may potentiate QT interval prolongation. QT prolongation is exacerbated, in particular, in the presence of bradycardia, hypokalemia, and congenital or acquired (i.e., drug induced) QT prolongation. (See also WARNINGS and ADVERSE REACTIONS.)

Unexpected, sudden deaths have occurred in hospitalized patients treated with phenothiazines. Previous brain damage or seizures may predispose. High doses should be avoided in known seizure patients. Sudden exacerbations of psychotic behavior patterns occurred in several patients shortly before death. Acute fulminating pneumonia or pneumonitis and aspiration of gastric contents also were observed. Therefore, the physician also should keep in mind the possible development of "silent pneumonias".

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 prescription of these drugs is contemplated in a patient with a 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 studies, nor epidemiologic studies conducted to date, however, have shown an association between chronic administration of these drugs and mammary tumorogenesis; the available evidence is considered too limited to be conclusive at this time.

Withdrawal Emergent Neurological Signs: Abrupt withdrawal after short-term administration of antipsychotic drugs does not generally pose problems. However, transient dyskinetic signs are experienced by some patients on maintenance therapy after abrupt withdrawal. The signs are very similar to those described under Tardive Dyskinesia, except for duration. Although it is not known whether gradual withdrawal of antipsychotic drugs will decrease the incidence of withdrawal emergent neurological signs, gradual withdrawal would appear to be advisable.

Older Patients: The incidence of adverse reactions may be greater in patients over 55 years of age since the half-lives of antipsychotic drugs are often prolonged. To minimize this possibility, the maintenance dosage should be reduced to the lowest effective level as soon as possible after initial titration and periodically reviewed.

Since psychiatric syndromes in the elderly can be caused by drugs or organic disease, withdrawal of the precipitating drug or treatment of the medical condition should supersede initiation of antipsychotic medication. These agents should not be used for non-psychiatric conditions for which other drugs are available, since the elderly are especially prone to develop adverse effects from antipsychotic drugs.

Children: Children with an acute febrile illness or suffering from dehydration seem to be much more susceptible than adults to neuromuscular reactions, particularly dystonias. In such patients, the drug should be used under close supervision and at low doses.

ADVERSE REACTIONS

Adverse reactions with different phenothiazines vary in type, frequency, and mechanism of occurrence, i.e., some are dose-related, while others involve individual patient sensitivity. Some adverse reactions may be more likely to occur with greater intensity, in patients with special medical problems.

Not all of the following adverse reactions have been observed with every phenothiazine derivative, but they have been reported with one or more and should be borne in mind when drugs of this class are administered:

Neurological: Extrapyramidal reactions including tremor, rigidity, akathisia, dystonia, dyskinesia, oculogyric crises, opisthotonos, hyperreflexia and sialorrhea. EEG changes, disturbed temperature regulation and seizures have also been encountered.

Persistent Tardive Dyskinesia: As with other antipsychotic agents, tardive dyskinesia may occur in patients on long-term therapy or may be observed after drug therapy has been discontinued. The risk seems to be greater in elderly patients on high doses, especially females. The symptoms are persistent and in some patients appear to be irreversible. The syndrome is characterized by rhythmical involuntary movements of the tongue, face, mouth or jaw (e.g., protrusion of tongue, puffing of cheeks, puckering of mouth, chewing movements). Sometimes, these may be accompanied by involuntary movements of the extremities.

There is no known effective treatment for tardive dyskinesia; antiparkinsonian agents usually do not alleviate the symptoms of this syndrome. It is suggested that all antipsychotic agents be discontinued if these symptoms appear. Should it be necessary to reinstitute treatment, or increase the dosage of the agent, or switch to a different antipsychotic agent, the syndrome 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. The physician may be able to reduce the risk of this syndrome by minimizing the unnecessary use of neuroleptic drugs and reducing the dose or discontinuing the drug, if possible, when manifestations of this syndrome are recognized, particularly in patients over the age of 50.

Behavioral: Sleep disturbances, drowsiness, fatigue, insomnia, and depression have been reported and may, in severe cases, necessitate reduction in dosage. As with other phenothiazine derivatives, reactivation or aggravation of psychotic processes may be encountered. Paradoxical effects such as agitation, anxiety, restlessness, excitement and bizarre dreams, have been observed.

Autonomic Nervous System: Dry mouth, nasal congestion, headache, nausea, constipation, tachycardia, hypotension, syncope, dizziness, blurred vision, vomiting, sweating, nasal congestion, and urinary incontinence have been observed.

Patients with pheochromocytoma, cerebral vascular or renal insufficiency, or a severe cardiac reserve deficiency such as mitral insufficiency appear to be particularly prone to hypotensive reactions with phenothiazine compounds, and should therefore be observed closely when the drug is administered. Should hypotension occur in patients receiving Stemetil (prochlorperazine) and a vasopressor agent be required i.v. norepinephrine or phenylephrine should be used, and not epinephrine, since phenothiazine derivatives can reverse the pressor effect of the latter drug.

Other autonomic reactions which have occurred with phenothiazines are salivation, polyuria, glaucoma, bladder paralysis, adynamic ileus, and fecal compaction.

Metabolic and Endocrine: Anorexia, menstrual irregularities, impotence, and increased thirst, weight changes, increased appetite, peripheral edema, galactorrhea, gynecomastia, and changes in libido have also occurred in patients receiving phenothiazine therapy.

Allergic or Toxic: Pruritus, dermatitis, rash, erythema, urticaria, seborrhea, eczema, exfoliative dermatitis, and photosensitivity. The possibility of an anaphylactoid reaction should be borne in mind.

Blood dyscrasias including leukopenia, agranulocytosis, pancytopenia, thrombocytopenic or non- thrombocytopenic purpura, eosinophilia, and anemia, have been associated with phenothiazine therapy. Routine blood counts are therefore advisable during prolonged therapy. If any soreness of the mouth, gums or throat or any symptoms of upper respiratory infection occur and confirmatory leukocyte count indicates cellular depression, therapy should be discontinued and other appropriate measures instituted immediately.

Cholestatic jaundice and biliary stasis may be encountered, particularly during the first months of therapy, and require immediate discontinuation of treatment.

Miscellaneous: The following adverse reactions have been reported in patients receiving phenothiazine derivatives : headache, asthma, laryngeal, cerebral and angioneurotic edema, altered cerebrospinal fluid proteins, systemic lupus erythematosus-like syndrome, hyperpyrexia, ECG and WEG changes and hypotension severe enough to cause fatal cardiac arrest. Skin pigmentation, epithelial keratopathy, lenticular, and corneal deposits have been associated with long-term administration.

Very rare cases of QT interval prolongation have been reported. There have been isolated reports of sudden death, with possible causes of cardiac origin (see WARNINGS and PRECAUTIONS) as well as cases of unexplained sudden death, in patients receiving neuroleptic phenothiazines.

Sudden, unexpected and unexplained deaths have been reported in hospitalized psychotic patients receiving phenothiazines. Previous brain damage or seizures may be predisposing factors; high doses should be avoided in known seizure patients. Several patients have shown flare-ups of psychotic behavior patterns shortly before deaths. Autopsy findings have usually revealed acute fulminating pneumonia or pneumonitis, aspiration of gastric contents or intramyocardial lesions.

Potentiation of CNS depressants (barbiturates, narcotics, analgesics, alcohol, antihistamines), may occur.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Symptoms: Primarily extrapyramidal reactions, CNS depression which may vary from simple lethargy to coma. Agitation and restlessness may also occur. Other possible manifestations include convulsions, fever and autonomic reactions such as hypotension, dry mouth and ileus.

Treatment: Essentially symptomatic and supportive. Early gastric lavage may be helpful.

Maintain an open airway. If hypotension occurs, the standard measures for managing circulatory shock should be initiated; if a pressor agent is required give norepinephrine or phenylephrine and not epinephrine as it may further depress the blood pressure. Extrapyramidal reactions should be treated with an antiparkinsonian agent.

Centrally, acting emetics will be ineffective because of prochlorperazine's antiemetic action. Limited experience indicates that phenothiazines are not dialyzable.

DOSAGE AND ADMINISTRATION

Begin with the lowest recommended dosage. Adjust to response of the individual.

ADULTS
Rectal route - To control nausea, vomiting or excessive anxiety : usually 5 to 10 mg, 3 or 4 times daily; in mild cases, a single dose of 5 to 10 mg is often adequate.

Parenteral route - I.M. Dosage: The drug is given by deep intramuscular injection. Total daily dosage rarely exceeds 40 mg, except in severe psychiatric cases. When control is achieved, the oral route should be substituted. To control nausea, vomiting or excessive anxiety: 5 to 10 mg, 2 or 3 times a day. In psychiatry, for the immediate control of severely disturbed patients, 10 to 20 mg initially, repeated every 2 to 4 hours until control is obtained. More than 3 or 4 doses are seldom necessary. The patients should be kept in bed and under medical supervision. In surgery : 5 to 10 mg I.M., 1 to 2 hours before anesthesia. Repeat once during surgery, if necessary. Post-operatively, the same dose of 5 to 10 mg I.M. may be given to control acute symptoms and

repeated, if necessary, every 3 to 4 hours (maximum, 40 mg daily).

I.V. Infusion: During and after surgery, Stemetil may be given I.V. in the infusion solution at a concentration of 20 mg per liter. Total daily dose rarely exceeds 30 mg.

CHILDREN

Daily dosage, administered in divided doses, should be based on body weight rather than on age, and should not be exceeded. Do not administer to children under 2 years of age or 9 kg of body weight. Occasionally the patient may react to the drug with signs of restlessness and excitement; if this occurs, treatment should be discontinued.

Parenteral route:

For severe nausea and vomiting, and in child psychiatry: calculate each dose on the basis of 0.13 mg/kg of body weight and give by deep I.M. injection. Control is usually obtained with one dose. When further therapy is needed, transfer the patient to an oral form at an equal or higher dose.

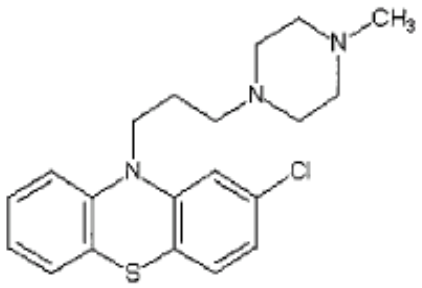
PHARMACEUTICAL INFORMATION

Drug substance

Proper name: Prochlorperazine

Chemical name: 2-chloro-10[3-(4-methyl-1-piperazinyl)propyl]-10H-phenothiazine

Structural formula:



Molecular formula: $C_{20}H_{24}ClN_3S$

Molecular weight: 373.94

Physical form: Clear, pale yellow, viscous liquid

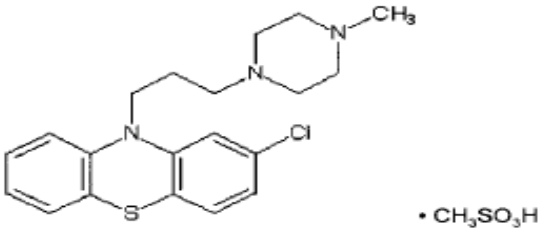
Solubility: Insoluble in water and freely soluble in alcohol, chloroform and ether.

Drug Substance

Proper name: Prochlorperazine mesylate

Chemical name: 2-chloro-10[3-(4-methyl-1-piperazinyl)propyl]-10H-phenothiazine mesylate

Structural Formula:



Molecular formula: $C_{20}H_{24}ClN_3S \bullet CH_3SO_3H$

Molecular weight: 566.2

Physical form: White or almost white powder

Solubility: Very soluble in water; sparingly soluble in alcohol; slightly soluble in chloroform; practically insoluble in ether.

pH: 2.0 to 3.0

Composition

Injectable: Each mL contains: prochlorperazine base 5 mg (as the mesylate). Non-medicinal ingredients: sodium chloride, sodium citrate, sodium sulphite anhydrous and water for injection.

Suppositories: Each rectal suppository contains: prochlorperazine base 10 mg. Non-medicinal ingredients: hydrogenated vegetable glycerides.

Stability and storage recommendations:
Stemetil (prochlorperazine) suppositories and Stemetil (prochlorperazine mesylate) injectable should be stored at 15° to 25°C. Protect from light.

AVAILABILITY OF DOSAGE FORMS

Stemetil (prochlorperazine base) 5 mg/mL (as mesylate) injectable is available in amber glass ampoules of 2 mL in boxes of 10 ampoules.

Stemetil (prochlorperazine base) 10 mg suppositories are available in boxes of 10 suppositories.

PHARMACOLOGY

The pharmacologic profile of prochlorperazine in experimental animals is similar to that of other phenothiazines. The following findings relate to animal studies in which prochlorperazine and chlorpromazine effects were compared on a drug weight basis. The sedative activity of prochlorperazine, based on the potentiating effects of ether anesthesia and morphine analgesia, is approximately one half that of chlorpromazine. The ability of prochlorperazine to block conditioned avoidance in rats is approximately one and a half times greater than chlorpromazine. The cataleptic effects of prochlorperazine are slightly greater than those of chlorpromazine but both compounds appear to be equi-effective in reducing motor activity.

The antiemetic effect of prochlorperazine, determined by the apoamorphine-induced vomiting in dogs, is four to six times greater than that of chlorpromazine. Chlorpromazine exerts more potent adrenergic and serotonin blocking effects and anticholinergic activity than does prochlorperazine.

In rats, prochlorperazine administered intraperitoneally distributes in all body tissues. The liver and spleen appear to store greater concentrations of the drug than other organs. Prochlorperazine enters the entero-hepatic circulation and is excreted chiefly in the feces. Less than 25 % of an intra peritoneal dose in rats is excreted in the urine.

TOXICOLOGY

Acute Toxicity

The following LD_{50} values have been obtained in mice for prochlorperazine.

- I.V. - 90 mg/kg
- S.C. - 400 mg/kg
- P.O. - 800 mg/kg

Subacute Toxicity

Administration of prochlorperazine to rats, 50 mg/kg P.O, daily for one month produced no disturbances of liver or kidney functions and no blood or bone-marrow alterations. All the animals survived without loss of weight, and appeared normal. Histological examination of kidney, liver, lung, and spleen did not reveal any toxic lesions.

In the dog, daily doses of 30 mg/kg for one month produced no mortality and all the animals appeared normal throughout treatment. They showed only a slight loss of weight, but no disturbances of liver or kidney functions. Histological examination revealed no abnormalities.

Teratogenicity

Prochlorperazine administered to pregnant rabbits and rats at dosage levels approximately 80 to 100 times the human therapeutic dose, produced no teratogenic effects.

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CONSUMER INFORMATION

PrSTEMETIL®
Prochlorperazine mesylate injection
Prochlorperazine Suppositories

This leaflet is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Stemetil®. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

Stemetil® is used to treat symptoms of psychotic disorders such as agitation, confusion, delusion, tension and anxiety.

Stemetil® is also used for the control of nausea and vomiting.

Ask your doctor if you have any questions about why Stemetil® has been prescribed to you.

What it does:

Stemetil® helps to:
- reduce and control psychotic symptoms
- control nausea and vomiting
- induce sleep

When it should not be used:

Do not use Stemetil® if you:

- Are allergic to Stemetil®, to phenothiazines (a type of antipsychotic) or to any of the ingredients in the product (see the section "**What the non-medicinal ingredients are"**)
- Have a sudden blood circulation failure or are in an altered state of consciousness or coma, especially if these were caused by alcohol or drugs
- Suffer from severe depression
- Have liver disease
- Have a blood disorder
- Have kidney problems
- Have pheochromocytoma (a tumour of the adrenal gland)
- Have severe heart or blood vessel disorders
- Have or have had brain damage
- Are taking high doses of drugs that cause you to sleep

Stemetil® is not indicated for use in children undergoing a surgery.

What the medicinal ingredient is:

Suppositories: Prochlorperazine

Injection: Prochlorperazine

What the nonmedicinal ingredients are:

Suppositories: hydrogenated vegetable glycerides

Injection: Sodium chloride, sodium citrate, sodium sulphite anhydrous and water for injection.

What dosage forms it comes in:

Suppositories 10 mg

Injection: 10 mg/2 mL prochlorperazine as prochlorperazine mesylate

WARNINGS AND PRECAUTIONS

At the beginning of treatment, Stemetil® may cause some people to become drowsy or less alert. You should not drive a car, operate machinery or participate in activities requiring alertness until you are sure Stemetil® does not affect you.

You should use extra care not to be exposed to extreme heat or some type of insecticides. Check with your doctor or pharmacist.

Children seem to be more susceptible than adult to some side effects. Stemetil® should not be used in children under 2 years old unless the doctor decides that Stemetil® is needed.

The incidence of adverse reactions may be greater in patients over 55 years of age. The lowest effective dose should be used to reduce the risk of having adverse reactions.

If you experience severe constipation and you are elderly, please consult your doctor as soon as possible.

Tardive dyskinesia, neuroleptic malignant syndrome cardiac, eye, skin and respiratory problems may occur in some patients taking Stemetil® (see the section **"SIDE EFFECTS AND WHAT TO**

DO ABOUT THEM").

Before using Stemetil®, tell your doctor if you:

- Have heart or blood vessel disease
- Have cerebrovascular (blood vessels of the brain) disorder
- Have constipation or intestinal blockage
- Have or have had a brain tumour or brain damage
- Suffer from an enlarged prostate (Benign Prostatic Hypertrophy)
- Suffer from an increase pressure within the eyes (glaucoma)
- Have or have had seizure disorders (e.g. epilepsy or have members of your family with seizure disorders)
- Have or have had breast cancer
- Plan to have surgery (or a procedure requiring anaesthetics)
- Are or are planning to become pregnant
- Are breast-feeding

During long-term treatment, blood, liver, and kidney tests should be done at regular intervals.

INTERACTIONS WITH THIS MEDICATION

Stemetil ® can add to the effects of alcohol. You should avoid consuming alcoholic beverages while on Stemetil ® therapy.

Before using any prescription, over-the-counter medicines or herbal products, check with your doctor or your pharmacist.

Stemetil ® can add to the effects of other drugs that cause drowsiness. Some examples of drugs that can cause drowsiness are:

- Drugs for allergies
- Drugs for insomnia
- Drugs for pain
- Drugs for seizure
- Drugs for depression
- Drugs for mental illness

Stemetil ® may cause a false pregnancy test result. Please check with your doctor if this happens.

PROPER USE OF THIS MEDICATION

Usual dose:

Your doctor has decided the best dose for you based on your individual situation and needs. It is important to take Stemetil® the way your doctor told you. Your doctor may increase or decrease your dose depending on your response.

You may experience side effects if the drug is stopped suddenly. Contact your physician before stopping your drug.

Adults

Rectal route: To control nausea, vomiting or anxiety, the usual dose is 5 to 10 mg, 3 or 4 times daily; in mild cases, a single dose of 5 to 10 mg is often adequate.

Injection in the muscle: Total daily dose rarely exceeds 40 mg, except in severe cases.

Injection in the vein: Stemetil® may be given as an injection in the vein during and after surgery. The Stemetil® injection formulation is diluted in a solution and injected slowly in a vein. Total daily dose rarely exceeds 30 mg.

Children

Stemetil® should not be given to children under 2 years of age or 9 kg of body weight. Occasionally, the children may react to the drug with signs of restlessness and excitement; if this occurs, treatment should be stopped.

Injection in the muscle
Stemetil® may be given as an injection in the muscle to control severe nausea and vomiting or in psychiatry. The dose is based on the body weight

Overdose:

If you have taken too much Stemetil®, immediately see your doctor or go to your nearest hospital emergency department. Do this even if there are no signs of discomfort or poisoning. The signs if you have taken too much Stemetil® may vary from drowsiness to coma. Agitation and restlessness may also occur. Other possible reactions include confusion, drowsiness, fever, low blood pressure, dry mouth and intestinal obstruction.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Stemetil®, like any medication, may cause some side effects. Discuss with your doctor if you do experience side effects.

Side effects include:

- Agitation, anxiety, bizarre dreams, dizziness, excitement, restlessness.
- Appetite changes, constipation, dizziness, dryness of the mouth, headache, increased thirst, nasal congestion, nausea, vomiting, sweating, urinary incontinence, weight changes.
- Changes in libido, impotence, increase of the breast size in men, lactation, menstrual irregularities, peripheral oedema (swelling of the legs, ankles, and feet).
- Your skin may be more sensitive to sunlight

Side effects that might need a reduction in your dose are:

- Drowsiness, fatigue, insomnia, sad mood, sleep disturbances.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect See text below for details		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Common	Extrapyramidal reactions[a)]		√	
Uncommon	Allergic Reactions[b)]			√
	Blood disorders[c)]		√	
	Cardiac disorders[d)]		√	
	Eye disorders[e)]		√	
	Liver disorders[c)]		√	
	Lung disorders[c)]		√	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

		Talk with your doctor or pharmacist		
	Neuroleptic malignant syndrome[f)]		√	
	Tardive dyskinesia[g)]		√	

a) Extrapyramidal reactions. The signs and symptoms of extrapyramidal reactions include tremor, muscle stiffness, body spasm, impairment of voluntary movement, upward eye rolling, exaggeration of reflexes or drooling. Tell your doctor if you experience any of these side effects. Your medication might have to be reduced.

b) Allergic Reactions:: You may develop an allergy to Stemetil® for example skin rash, redness or itching. Consult your doctor immediately if you develop an allergy to Stemetil®.

c) Blood, liver and lung disorders have been associated with this class of drug. It is important that you tell your doctor at once about any unexplained symptom you might experience. Examples of this are soreness of the mouth, gums or throat or any symptoms of upper respiratory infection, unexplained fever, itching, flu-like symptoms, coughing, abdominal pain, jaundice.

d) Cardiac disorders: Low blood pressure and fainting have been reported. Uncommonly, Stemetil® may cause the heartbeat to become faster or irregular. Check immediately with your doctor if these side effects occur.

e) Eye disorders: Blurred vision has been observed. Other eye disorders are reported, specifically after long-term administration. Consult you doctor if you experience any vision problems.

f) Neuroleptic malignant syndrome:Another possible serious unwanted effect is the neuroleptic malignant syndrome. Signs and symptoms of the neuroleptic malignant syndrome include severe muscle stiffness, increased sweating, fever, fast or irregular heartbeat, high or low blood pressure, difficult or fast breathing and confusion. If any of the above side effects occur, consult your doctor immediately.

g) Tardive dyskinesia may occur in some patients on long-term therapy or after they stop using Stemetil®. Signs of tardive dyskinesia include muscle twitching or uncontrolled movements of the mouth, tongue, face or jaw (e.g., protrusion of tongue,

puffing of cheeks, puckering of mouth, chewing movements). Sometimes, these may be accompanied by involuntary movements of the extremities. In some patients, this side effect may not go away after they stop using Stemetil®. These effects are rare and usually appear only after long-term therapy at high doses. Elderly patients may be at higher risk. Tell your doctor immediately if you experience any muscle twitching or abnormal body movements.

This is not a complete list of side effects. For any unexpected effects while taking Stemetil®, contact your doctor or pharmacist.

HOW TO STORE IT

Stemetil® suppositories and injection should be stored at room temperature between 15°C and 25°C.

Protect from exposure to light.

Keep out of reach of children.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada collects information on serious and unexpected effects of drugs . If you suspect you have had a serious or unexpected reaction to this drug you may notify Health Canada by:

toll-free telephone: 866-234-2345
toll-free fax 866-678-6789
By email: cadrmp@hc-sc.gc.ca

By regular mail:
National AR Centre
Marketed Health Products Safety and Effectiveness Information Division
Marketed Health Products Directorate
Tunney's Pasture, AL 0701C
Ottawa ON K1A 0K9

NOTE: Before contacting Health Canada, you should contact your physician or pharmacist.

MORE INFORMATION

Your physician, nurse and pharmacist are always your best source of information about your condition and treatment. If you have additional questions or concerns, be sure to ask them.

This document plus the full product monograph is available upon request to the sponsor, sanofi-aventis Canada Inc., 2150 St Elzear Blvd. West , Laval , Quebec H7L 4A8, at:
1-800-265-7927

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