

PRODUCT INFORMATION

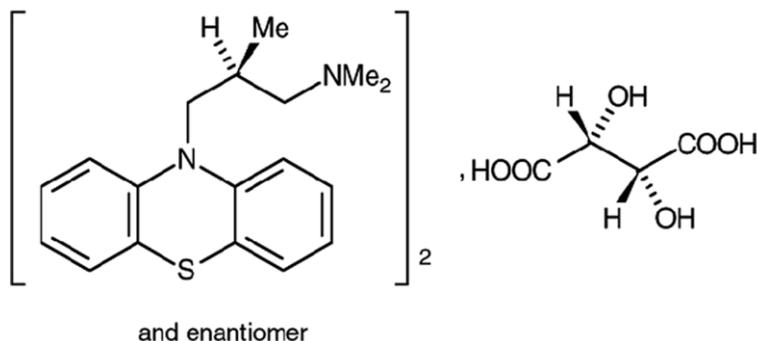
VALLERGAN®

NAME OF THE MEDICINE

Non-proprietary Name

Alimemazine (trimeprazine) tartrate

Chemical Structure



CAS Number

4330-99-8

DESCRIPTION

Alimemazine (trimeprazine) tartrate is (*RS*)-dimethyl (2-methyl -3-phenothiazin-10-ylpropyl) amine (*2R,3R*)-tartrate. It contains not less than 99% and not more than 101% of $(C_{18}H_{22}N_2S)_2, C_4H_6O_6$, calculated with reference to the dried substance. Alimemazine (trimeprazine) tartrate is a white or slightly cream powder which darkens on exposure to light. It is freely soluble in water and sparingly soluble in ethanol (96%).

Vallergan Syrup contains 7.5 mg alimemazine (trimeprazine) tartrate in 5 mL. The inactive ingredients are 68% w/v of sucrose, ethanol, sodium citrate dihydrate, sodium sulfite, sodium metabisulfite, sodium benzoate, citric acid, ascorbic acid, caramel and apricot flavour 91.

Vallergan Forte Syrup contains 30 mg alimemazine (trimeprazine) tartrate in 5 mL. The inactive ingredients are 68% w/v of sucrose, ethanol, sodium citrate dihydrate, sodium sulfite, sodium metabisulfite, sodium benzoate, citric acid, ascorbic acid, and apricot flavour 91.

Vallergan Tablets contain 10 mg alimemazine (trimeprazine) tartrate. The inactive ingredients are acacia, brilliant blue FCF, erythrosine, magnesium stearate, polyvinyl acetate, colloidal anhydrous silica, wheat starch and sucrose.

PHARMACOLOGY

Pharmacokinetic properties

There is little information about blood levels, distribution and excretion in humans. The rate of metabolism and excretion of phenothiazines decreases in old age.

Pharmacodynamic properties

Alimemazine (trimeprazine) tartrate has a central sedative effect, comparable to that of chlorpromazine, but largely devoid of the latter's anti-adrenaline action.

It has powerful antihistaminic, anti-emetic, antipruritic and sedative actions.

INDICATIONS

Urticaria

Vallergan is used for the oral treatment of pruritus irrespective of the cause. The pruritus of self limiting conditions such as sunburn, photosensitivity, measles and chickenpox, is markedly relieved in 24 to 48 hours.

Pruritus unaffected by other therapies is often relieved by Vallergan. Its use frequently allows reduction or elimination of concurrent local and systemic treatment; this is probably due to interruption of the itch, scratch, itch cycle, which encourages the healing of lesions.

The sedation produced by alimemazine (trimeprazine) tartrate is of value, particularly when the itching appears to be associated with emotional stress or nervous tension.

Vallergan has been found to be useful in children as a general sedative.

CONTRAINDICATIONS

Alimemazine (trimeprazine) tartrate should be avoided in patients with hepatic or renal dysfunction, epilepsy, Parkinson's disease, hypothyroidism, phaeochromocytoma, myasthenia gravis and prostatic hypertrophy. It should be avoided in patients known to be hypersensitive to phenothiazines or to any of the excipients. It should be avoided in patients with a history of narrow angle glaucoma or with a history of agranulocytosis.

Vallergan is contraindicated for use in children less than 2 years of age.

PRECAUTIONS

QT interval prolongation has been reported with phenothiazines.

Alimemazine (trimeprazine) tartrate should be used with caution in:

elderly or volume depleted patients who are more susceptible to orthostatic hypotension

elderly patients presenting chronic constipation (risk of paralytic ileus)

elderly patients with possible prostatic hypertrophy

elderly patients in hot and cold weather (risk of hyper/hypothermia)

patients with certain cardiovascular diseases, due to the tachycardia-inducing, arrhythmia-inducing and hypotensive effects of phenothiazines

Patients are strongly advised not to consume alcoholic beverages or medicines containing alcohol throughout treatment.

Exposure to sunlight should be avoided during treatment.

Caution must be exercised in patients with a history of seizures.

The sugar content of Vallergan Syrup and Vallergan Forte Syrup should be considered in patients with diabetes or on low sugar diets.

This medicine contains sulfites that may cause or exacerbate anaphylactic reactions.

There is a risk of post-operative restlessness especially if the child is in pain.

Use in pregnancy (Category C)

There are limited data on the use of alimemazine (trimeprazine) tartrate in pregnant women. Alimemazine (trimeprazine) tartrate, like other drugs, should be avoided in pregnancy unless the physician considers it essential.

When given in high doses during late pregnancy, phenothiazines have caused prolonged extrapyramidal disturbances in the child. Neuroleptics may occasionally prolong labour and at such time, should be withheld until the cervix is dilated 3-4 cm. Possible adverse effects on the neonate include lethargy or paradoxical hyperexcitability, tremor and low Apgar score.

Some phenothiazines have shown evidence of harmful effects in animals.

Use in lactation

Phenothiazines may be excreted in milk. Breastfeeding should be suspended during treatment.

Paediatric use

Vallergan is contraindicated for use in children less than 2 years of age due to the risk of marked sedation and respiratory depression.

Use in the elderly

Dosage should be reduced to 10 mg once or twice daily.

Effects on ability to drive and use machines

Patients should be warned about drowsiness during the early days of treatment, and advised not to drive or operate machinery.

INTERACTIONS WITH OTHER MEDICINES

The sedative effects of phenothiazines may be intensified (additively) by alcohol, anxiolytics and hypnotics, opiates, barbiturates and other sedatives. There may be increased antimuscarinic and sedative effects of phenothiazines with tricyclic antidepressants and monoamine oxidase inhibitors (MAOIs), including moclobemide. Respiratory depression may occur.

The hypotensive effect of most antihypertensive drugs, especially alpha adrenoreceptor blocking agents, may be exaggerated by phenothiazines. The use of antimuscarinics in conjunction with antihistamines will increase the risk of antimuscarinic side effects.

The mild anticholinergic effect of phenothiazines may be enhanced by other anticholinergic drugs, possibly leading to constipation, heat stroke, etc.

The action of some drugs may be opposed by phenothiazines. These include amphetamine, levodopa, clonidine, guanethidine and adrenaline.

Anticholinergic agents may reduce the antipsychotic effect of phenothiazines.

Some drugs interfere with absorption of phenothiazines: antacids, anti-Parkinson agents, lithium. Increases or decreases in the plasma concentrations of a number of drugs, e.g. propranolol, phenobarbitol, have been observed but were not of clinical significance.

High doses of phenothiazines reduce the response to hypoglycaemic agents, the dosage of which may have to be raised. Adrenaline must not be used in patients overdosed with phenothiazines.

ADVERSE EFFECTS

The most common side effect is drowsiness occurring in the early stages of treatment. This can be minimised by giving the major portion of the dosage at bedtime and taking daytime doses directly after meals, when this is practicable.

Minor side effects are nasal stuffiness, dry mouth, insomnia and agitation. In long term use, dry mouth may cause damage to teeth and oral mucous membranes.

Constipation, dizziness, headache and retention of urine have been reported.

Liver function

Jaundice, usually transient, occurs in a very small percentage of patients. A premonitory sign may be a sudden onset of fever after one to three weeks of treatment, followed by the development of jaundice. Neuroleptic jaundice has the biochemical and other characteristics of obstructive jaundice and is associated with obstructions of the canaliculi by bile thrombi; the frequent presence of an accompanying eosinophilia indicates the allergic nature of this phenomenon. Treatment should be withheld on the development of jaundice.

Cardiorespiratory

Hypotension or pallor may occur in children. Elderly or volume depleted subjects are particularly susceptible to postural hypotension.

Cardiac arrhythmias, including atrial arrhythmia

Atrioventricular (AV) block, ventricular tachycardia and fibrillation have been reported during therapy, possibly related to dosage. Pre-existing cardiac disease, old age, hypokalaemia and concurrent tricyclic antidepressants may predispose. Electrocardiograph (ECG) changes, usually benign, include widened QT interval, ST depression, U-waves and T-wave changes.

Respiratory depression is possible in susceptible patients.

Blood picture

A mild leukopaenia occurs in up to 30% of patients on prolonged high dosage. Agranulocytosis may occur rarely; it is not dose related. The occurrence of unexplained infections or fever requires immediate haematological investigation.

Extrapyramidal

Acute dystonias or dyskinesias, usually transitory, are more common in children and young adults and usually occur within the first 4 days of treatment or after dosage increases.

Akathisia characteristically occurs after large doses.

Parkinsonism is more common in adults and the elderly. It usually develops after weeks or months of treatment. One or more of the following may be seen: tremor, rigidity, akinesia or other features of Parkinsonism. Commonly, just tremor is seen.

The occurrence of tardive dyskinesia, if it occurs, is usually, but not necessarily, after prolonged or high dosage. It can occur after treatment has been stopped. Dosage should therefore be kept low whenever possible.

Skin and eyes

Contact skin sensitisation is a serious but rare complication in those frequently handling preparations of phenothiazines. Care must be taken to avoid contact of the drug with the skin. Skin rashes of various kinds may also be seen in patients treated with alimemazine (trimeprazine) tartrate. Patients on high dosage may develop photosensitivity in sunny weather and should avoid exposure to direct sunlight. Ocular changes and the development of a metallic greyish-mauve colouration of exposed skin have been noted in some individuals, mainly females, who have received chlorpromazine continuously for long periods (four to eight years). Accommodation disorder has also been reported.

Endocrine

Hyperprolactinaemia, which may result in galactorrhoea, gynaecomastia, amenorrhoea and impotence, may occur.

Neurological effects

Neuroleptic malignant syndrome (hyperthermia, rigidity, autonomic dysfunction and altered consciousness) may occur.

Paradoxical excitement has been noted.

Nervous system disorders

Convulsions have been reported.

DOSAGE AND ADMINISTRATION

For all uses of Vallergran, DO NOT exceed the recommended dose.

Urticaria

Adults

10 mg (approximately 6.5 mL of Vallergran Syrup; approximately 1.6 mL of Vallergran Forte Syrup) three or four times daily is sufficient in most cases, although up to 100 mg in one day has been used in intractable cases.

Children

Vallergran is contraindicated for use in children less than 2 years of age due to the risk of marked sedation and respiratory depression.

In children 2 years of age and older, 2.5 to 5 mg three or four times daily; when additional sedation is needed, especially in infantile eczema, a dose of 22 mg/day has been recommended.

Higher dosage (up to 30 mg twice daily) has been used in the treatment of infantile eczema. This dosage is administered as Vallergran Forte Syrup containing alimemazine (trimeprazine) tartrate 30 mg/5 mL.

Where necessary, treatment may be continued for months without loss of efficiency. The administration of alimemazine (trimeprazine) tartrate does not antagonise specific therapy and, in extremely pruritic inflammatory conditions, may be associated with the use of emulsificans aquosum baths, the local application of hydrocortisone or other measures.

Sedation

Children

3 to 6 years: 2.5 to 10 mL of Vallergran Forte Syrup (15 to 60 mg) per day in divided doses

7 to 12 years: 10 to 15 mL of Vallergran Forte Syrup (60 to 90 mg) per day in divided doses.

OVERDOSAGE

Symptoms of phenothiazine overdose include drowsiness or loss of consciousness, hypotension, tachycardia, ECG changes, ventricular arrhythmias and hypothermia. Severe extra-pyramidal dyskinesias may occur.

Generalised vasodilatation may result in circulatory collapse. Raising the patient's legs may suffice. In severe cases, volume expansion by intravenous fluids may be needed. Infusion fluids should be warmed before administration in order not to aggravate hypothermia.

Positive inotropic agents such as dopamine may be tried if fluid replacement is insufficient to correct the circulatory collapse. Peripheral vasoconstrictor agents are not generally recommended. Avoid the use of adrenaline.

Ventricular or supraventricular tachy-arrhythmias usually respond to restoration of normal body temperature and correction of circulatory or metabolic disturbances. If persistent or life-threatening, appropriate anti-arrhythmic therapy may be considered. Avoid lignocaine and, as far as possible, long acting anti-arrhythmic drugs.

Pronounced central nervous system depression requires airway maintenance or, in extreme circumstances, assisted respiration. Convulsions should be treated with intravenous diazepam.

Neuroleptic malignant syndrome has been reported in the context of alimemazine (trimeprazine) tartrate overdose. Symptoms include a combination of hyperthermia, muscle rigidity, altered mental status and autonomic instability. Since this syndrome is potentially fatal, the use of Vallergran must be discontinued immediately, and intensive clinical monitoring and symptomatic treatment must be initiated.

Neuroleptic malignant syndrome should be treated with cooling. Dantrolene sodium may be tried.

Strict adherence to the recommended dose is critical.

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

PRESENTATION AND STORAGE CONDITIONS

♦Vallergan Syrup is a clear, bright, straw coloured, apricot flavoured liquid containing 7.5 mg alimemazine (trimeprazine) tartrate in 5 mL. Each bottle contains 100 mL. Store below 25°C. Protect from light.

♦Vallergan Forte syrup is a clear, colourless to pale yellow coloured, apricot flavoured liquid containing 30 mg alimemazine (trimeprazine) tartrate in 5 mL. Each bottle contains 100 mL. Store below 25°C. Protect from light.

Vallergan Tablets are dark blue, sugar coated tablets marked with M & B containing 10 mg of alimemazine (trimeprazine) tartrate. Each pack contains 50 tablets. Store below 25°C. Protect from light.

NAME AND ADDRESS OF THE SPONSOR

sanofi-aventis australia Pty Ltd
12-24 Talavera Road
Macquarie Park NSW 2113
Australia

POISON SCHEDULE OF THE MEDICINE

♦Syrup: Pharmacist Only Medicine (S3)

Tablets: Pharmacist Only Medicine (S3)

♦Forte Syrup: Prescription Only Medicine (S4)

♦ Marketed presentations

DATE OF FIRST INCLUSION IN THE ARTG

21 October 1991

DATE OF MOST RECENT AMENDMENT

26 July 2017