SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Alimemazine tartrate 7.5mg/5ml Syrup

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml dose contains 1.5mg of alimemazine tartrate.

Excipients with known effect:

Sucrose	680.0 mg/ml
Sodium sulphite anhydrous (E221)	1.0 mg/ml
Sodium Metabisulphite (E223)	1.0 mg/ml
Sodium Benzoate	1.0 mg/ml
Ethanol	40.2 mg/mL

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Syrup

Clear, colourless to pale yellow, syrupy liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Alimemazine has a central sedative effect comparable to that of chlorpromazine but largely devoid of the latter's anti adrenaline action.

In children aged 3-7 years:

• Pre-medication sedation before general anaesthesia

Adults and children aged 3 years and over:

• Second-line treatment in the symptomatic relief of urticaria and pruritus.

4.2 Posology and method of administration

Posology

Paediatric population: Not recommended for children less than 3 years old (

see also sections 4.3 and 4.4).

Do NOT exceed the recommended dose (see also section 4.9).

Urticaria and pruritus

Adults: 10 mg (approx. 6.5 ml) two or three times daily; up to 100 mg per day have been used in intractable cases.

Elderly: Dose should be reduced to 10 mg (approx. 6.5 ml) once or twice daily.

Children over 3 years of age: 2.5 – 5 mg (approx. 1.7 – 3.3 ml) three or four times daily.

Sedative premedication before general anaesthesia

(Children aged 3-7 years:) the maximum dosage recommended is 2mg (approx. 1.3ml) per kg bodyweight 1-2 hours before the operation.

Method of administration:

For oral administration.

4.3 Contraindications

Alimemazine is contraindicated in patients with:

- Known hypersensitivity to phenothiazines or to any of the excipients listed in section 6.1.
- Use in patients with hepatic or renal dysfunction, epilepsy, Parkinson's disease, hypothyroidism, phaeochromocytoma, myasthenia gravis, and prostatic hypertrophy.
- Use in patients with history of narrow angle glaucoma and agranulocytosis.
- Use in children less than 3 years of age (see Section 4.4).

4.4 Special warnings and precautions for use

Patients are strongly advised not to consume alcoholic beverages or medicines containing alcohol throughout treatment (see section 4.5).

Exposure to sunlight should be avoided during treatment (see section 4.8).

Alimemazine should be used with caution in:

- Elderly or volume depleted patients who are more susceptible to orthostatic hypotension (see section 4.8)
- Elderly patients presenting chronic constipation (risk of paralytic ileus),
- Elderly patients with possible prostatic hypertrophy (see section 4.3);
- Elderly patients in hot and cold weather (risk of hyper/hypothermia) (see section 4.8)
- Patients with certain cardiovascular diseases, alimemazine may cause arrhythmias due to the tachycardia-inducing and hypotensive effects of phenothiazines (see section 4.8)
- Patients with seizures (see section 4.8).

Paediatric population:

Alimemazine is contraindicated for use in children less than 3 years of age due to the risk of marked sedation and respiratory depression.

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

Alimemazine Syrup contains:

Sucrose: Patients with rare hereditary problems of fructose intolerance, glucose galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Ethanol: 81mg of alcohol (ethanol) in each 2ml which is equivalent to 40.5mg/ml (4% w/v). The amount in 2ml of this medicine is equivalent to less than 2ml beer and 1ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.

Sodium sulphite (E221) and sodium metabisulphite (E223) these may rarely cause severe allergic hypersensitivity reactions and bronchospasm.

This medicinal product contains 24.36 mg sodium per 5ml, equivalent to 1.17% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicinal products and other forms of interaction

The sedative effects of phenothiazines may be intensified (additively) by alcohol (see section 4.4), anxiolytics and hypnotics, opiates, barbiturates and other sedatives. There may be increased antimuscarinic and sedative effects of phenothiazines with tricyclic antidepressants and MAOI's (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 will increase the risk of antimuscarinic side effects when in conjunction with antihistamines.

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

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

Anticholinergic agents may reduce the antipsychotic effect of phenothiazines.

Some drugs interfere with absorption of phenothiazines: antacids, anti-Parkinson, and lithium. Increases or decreases in the plasma concentrations of a number of drugs, e.g. propranolol and phenobarbital 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.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data from the use of Alimemazine tartrate in pregnant women, but it has been widely used for many years without apparent ill consequence. Some phenothiazines have shown evidence of harmful effects in animals. Alimemazine, like other drugs, should be avoided in pregnancy unless the physician considers it essential. Neuroleptics may occasionally prolong labour and at such a time should be withheld until the cervix is dilated 3-4cm. Possible adverse effects on the neonate include lethargy or paradoxical hyper excitability, tremor and low Apgar score.

Breast-feeding

Phenothiazines may be excreted in human milk. Breast feeding should be discontinued during treatment with alimemazine tartrate.

Fertility

There are no fertility data available.

4.7 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.

4.8 Undesirable effects

The following adverse reactions are classified by system organ class and ranked under heading of frequency using the following convention:

Not known (cannot be estimated from the available data).

Blood and lymphatic system disorders:

- A mild leukopenia 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.

Psychiatric disorders:

- Insomnia
- Agitation.

Nervous system disorders:

- Drowsiness.
- Dizziness
- Headache
- Convulsions have been reported in some patients.
- Extrapyramidal effects such as: Acute dystonias or dyskinesias, usually transitory are commoner 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 commoner 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).

– Tardive dyskinesia: If this occurs it is usually, but not necessarily, after prolonged or high dosage. It can even occur after treatment has been stopped. Dosage should therefore be kept low whenever possible.

Eye disorders:

- Accommodation disorders

Cardiac disorders:

Cardiac arrhythmias, including atrial arrhythmia, atrioventricular (A-V) block, ventricular tachycardia and fibrillation have been reported during therapy, possibly related to dosage (see section 4.4). Pre-existing cardiac disease, old age, hypokalaemia and concurrent tricyclic antidepressants may predispose.

Vascular disorders:

- Hypotension, or pallor may occur in children.
- Elderly or volume depleted subjects are particularly susceptible to postural hypotension (see section 4.4).

Respiratory, thoracic and mediastinal disorders:

- Nasal congestion
- Respiratory depression is possible in susceptible patients.

Gastrointestinal disorders:

- Dry mouth
- Constipation

Hepatobiliary disorders:

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.

Skin and subcutaneous tissue disorders:

- 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 the drug.
- Patients on high dosage may develop photosensitivity in sunny weather and should avoid exposure to direct sunlight (see section 4.4). 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).

Renal and urinary disorders:

- Urinary retention

Endocrine disorders:

- Hyperprolactinaemia which may result in galactorrhoea, gynaecomastia, amenorrhoea and impotence.
- Neuroleptic malignant syndrome (hyperthermia, rigidity, autonomic dysfunction and altered consciousness) may occur (see section 4.9).

General disorders and administration site conditions:

- Paradoxical excitement has been noted.

Investigations:

ECG changes, usually benign, including:

- QT interval prolongation
- ST segment depression
- U-wave abnormality
- T-wave abnormality

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms

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

Treatment

If the patient is seen sufficiently soon (up to 6 hours) after ingestion of a toxic dose, gastric lavage may be attempted. Pharmacological induction of emesis is unlikely to be of any use. Activated charcoal should be given. There is no specific antidote. Treatment is supportive.

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 lidocaine and, as far as possible, long acting anti-arrhythmic drugs.

Pronounced central nervous system depression requires airway maintenance or, in extreme circumstances, assisted respiration. Severe dystonic reactions usually

respond to procyclidine (5-10mg) or orphenadrine (20-40mg) administered intramuscularly or intravenously. Convulsions should be treated with intravenous diazepam.

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

Strict adherence to the recommended dose is critical (see also section 4.2)

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: R06A D01

Pharmacotherapeutic group: Phenothiazine derivatives, Antihistamines for systemic use

Alimemazine has a central sedative effect, comparable to that of chlorpromazine, but largely devoid of the latter's anti-adrenaline action. It has powerful antihistamine and anti-emetic actions.

5.2 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.

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose

Ethanol

Citric acid monohydrate, anhydrous (E330)

Sodium benzoate (E211)

Sodium sulphite anhydrous (E221)

Sodium metabisulphite (E223)

Ascorbic acid (E300)

Apricot Flavour

Caramel Flavour

Sodium citrate (E331)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years.

1 month after first opening

6.4 Special precautions for storage

Store in the original package in order to protect from light.

6.5 Nature and contents of container

100ml Amber glass bottle with a white tamper evident child-resistant plastic cap. A 2 ml graduated dosing syringe and syringe adapter are also provided.

6.6 Special precautions for disposal

Not applicable

7 MARKETING AUTHORISATION HOLDER

Mercury Pharmaceuticals Ltd,
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London, EC2M 1QS,
UK

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PL 12762/0535

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