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.

Also contains

Sucrose	680 mg/ml
Sodium sulphite anhydrous (E221)	1.0 mg/ml
Sodium metabisulphite (E223)	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 powerful antihistamine and anti-emetic actions and is used in the management of urticaria and pruritus. Alimemazine tartrate 7.5mg / 5ml syrup should be used for this indication in children.

Alimemazine may be used in pre-medication as a sedative before anaesthesia in children aged between 2 to 7 years. Alimemazine tartrate 30 mg / 5ml syrup can be used for the specific indication of pre-anaesthesia sedation in children (see Section 4.2).

4.2 Posology and method of administration

For oral use

Not recommended for infants less than 2 years old.
Do NOT exceed the recommended dose (see also section 4.9).

Children over 2 years of age:
Urticaria and pruritus
Aged 2 – 5 years: 2.5mg (1.7ml) three to four times per day
Aged 5 – 12 years: 5mg (3.3ml) three to four times per day

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

For the indication of sedation prior to anaesthesia, which requires a once only, high dose of alimemazine, the higher strength (30mg/5ml) syrup should be prescribed in order to limit ethanol exposure (see Section 4.4).

A 2 ml graduated syringe is provided for accurate dosing.

4.3 Contraindications

Use in patients with hepatic or renal dysfunction, epilepsy, Parkinson's disease, hypothyroidism, phaeochromocytoma, myasthenia gravis, and prostatic hypertrophy.

Use in patients known to be hypersensitive to phenothiazines or to any of the excipients listed in section 6.1 or with history of narrow angle glaucoma.

Use in children less than 2 years of age (see Section 4.4 Special warnings and precautions for use).

4.4 Special warnings and precautions for use

Precautions for use:

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, due to the tachycardia-inducing and hypotensive effects of phenothiazines (see section 4.8).

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

Paediatric population:

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

Alimemazine Syrup contains 5% ethanol (alcohol) i.e. up to 81mg ethanol per 2ml dose. This is equivalent to 2ml beer and less than 1ml wine per dose. This can be harmful for those suffering from alcoholism. To be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients with liver disease or epilepsy.

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

Exposure to sunlight should be avoided during treatment (see section 4.8).
Phenothiazines should be used with particular care in the presence of extremes of temperature because of its capacity to interfere with the body’s thermoregulator.

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

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 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, 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.

As with other neuroleptic phenothiazines, caution is advised with concomitant use of QT prolonging drugs or drugs that cause electrolyte imbalance.

4.6 Fertility, pregnancy and lactation

There is inadequate evidence of the safety of Alimemazine in human pregnancy, 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. Phenothiazines may be excreted in milk: breast feeding should be suspended during treatment.

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

Minor side-effects are nasal stuffiness, insomnia, agitation.

Anticholinergic effects such as dry mouth and urinary retention.

Central effects such as drowsiness or sedation, more marked at the start of treatment.

Convulsions have been reported in some patients.

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 (see section 4.4).

Cardiac arrhythmias, including atrial arrhythmia: A-V 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. 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 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.

Extrapyramidal: 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.

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 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).

Endocrine: hyperprolactinaemia which may result in galactorrhoea, gynaecomastia, amenorrhoea: impotence.

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

Paradoxical excitement has been noted.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

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

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

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

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Ethanol
Citric acid anhydrous (E300)
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 opening

6.4 Special precautions for storage

Store in 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 and other handling

The adaptor is inserted in the bottle before use. The pipette is then put in the adaptor in the upright position and then turned upside down together with the bottle (Fig. 1). In this position the medicine is dosed. At the start of the measuring procedure, the transparent dosing body as well as the white plunger must be in the bottommost position. To measure the dosing quantity, use one hand to hold the bottom, transparent dosing body and the other hand to pull on the top, white plunger until you can read the desired quantity in ml.

Fig. 1

Afterwards the bottle is turned in the upright position again and the dosed pipette can be removed (Fig. 2). The bottle is sealed after removing the inserted adaptor by using the common closure.

Fig. 2

7 MARKETING AUTHORISATION HOLDER

Mercury Pharmaceuticals (Ireland) Ltd
4045 Kingswood Road
Citywest Business Park
Co Dublin
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0073/153/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30th January 2015

10 DATE OF REVISION OF THE TEXT

September 2017