SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Alfresed 7.5mg/5ml Syrup

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml of syrup contains 7.5mg alimemazine tartrate.

Excipients with known effect:

Each 5ml of syrup contains 3400mg sucrose, 2mg methyl parahydroxybenzoate (E218), 5mg sodium sulfite anhydrous (E221) and 5mg sodium metabisulfite (E223).

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Syrup

A clear, colourless to pale yellow syrupy liquid with caramel odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

Alfresed is used as the second line treatment in the symptomatic relief of urticaria and pruritus for adults and children 3 years and above.

Alfresed may be used in pre-medication as a sedative before anaesthesia in children aged between 3 to 7 years.

4.2 Posology and method of administration

Posology
Not recommended for infants less than 3 years old (see also sections 4.3 and 4.4).

DO NOT exceed the recommended dose (see section 4.9).

Urticaria and pruritus
Adults: 10mg (approx. 6.7ml) two or three times daily; up to 100mg per day have been used in intractable cases.

Elderly: dosage should be reduced to 10mg (approx. 6.7ml) once or twice daily.

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

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

When administration of small volumes is required, Alfresed syrup of a higher strength (30mg/5ml) is recommended for the indication of sedation prior to anaesthesia.

Method of administration
For oral administration.

4.3 Contraindications

Alfresed should be avoided in patients with hepatic or renal dysfunction, epilepsy, Parkinson's disease, hypothyroidism, phaeochromocytoma, myasthenia gravis, prostatic hypertrophy. It should be avoided 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, history of agranulocytosis.

Alfresed is contraindicated for use in children less than 3 years of age (see section 4.4).

4.4 Special warnings and precautions for use

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).

Alfresed 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:
Alfresed 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.

Excipient Warnings
This product contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. This should be taken into account in patients with diabetes mellitus. The sucrose may be harmful to the teeth if this medicine is taken for long-term use e.g. for two weeks or more.

This product also contains methyl parahydroxybenzoate (E218), which may cause allergic reactions (possibly delayed).

This product also contains sodium sulfite anhydrous (E221) and sodium metabisulfite (E223), which may rarely cause severe hypersensitivity reactions and bronchospasm.

This medicine contains less than 1mmol sodium (23mg) per 5ml, that is to say essentially 'sodium-free'.

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 used in conjunction with antihistamines.

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.

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

Some drugs interfere with absorption of phenothiazines: antacids, anti-Parkinson and lithium. Increases or decreases in the plasma concentrations of a number of drugs, eg propranolol, 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 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 hyperexcitability, tremor and low Apgar score.

Breast-feeding

Phenothiazines may be excreted in milk: breast feeding should be suspended during treatment.

Fertility

Animal studies are insufficient with respect to effect on fertility. However, some phenothiazines show adverse effects on fertility.

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

Gastrointestinal disorders:

- Constipation
- Dry mouth

Respiratory, thoracic and mediastinal disorders:

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

Psychiatric disorders:

- Insomnia
- Agitation

Hepatobilliary 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.

Renal and urinary disorders:

- Retention of urine

Vascular disorders:

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

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

Investigation:
ECG changes, usually benign, include widened QT interval, ST depression, U-waves and T-wave changes.

Eye disorders:
- Accommodation disorders

Blood and lymphatic system disorders:
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.

Nervous system disorders:
- 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.
- Convulsions have been reported in some patients.
- Dizziness
- Headache
- Drowsiness

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).

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.

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 Website at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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 antiarrhythmic 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 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: Antihistamines; 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

Citric acid monohydrate

Sodium citrate

Methyl parahydroxybenzoate (E218)

Sodium sulfite anhydrous (E221)

Sodium metabisulfite (E223)

Ascorbic acid

Caramel flavour

Apricot flavour

Purified water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

Discard 30 days after first opening.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Bottle: Type III amber glass bottle

Closure: Tamper evident, child resistant white plastic cap with polypropylene inner, polyethylene outer and expanded polyethylene (EPE) liner.

Dosing Device: 5ml oral syringe with 0.1ml graduation consists of clear polypropylene barrel and white coloured polyethylene plunger and low density polyethylene (LDPE) syringe adaptor

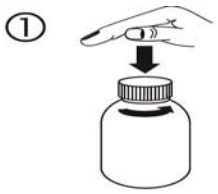
Pack size: 100ml

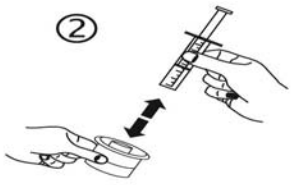
6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

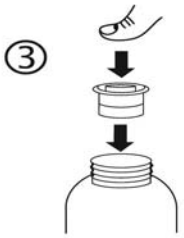
Instructions for the use of syringe:

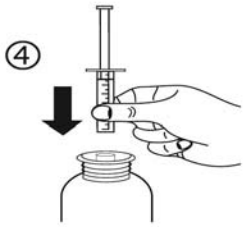
1. Open the bottle: press the cap and turn it anticlockwise (figure 1). Separate the adaptor from the syringe (figure 2).



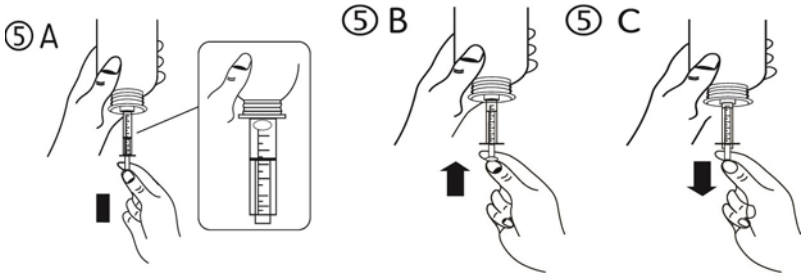


2. Insert the adaptor into the bottle neck (figure 3). Ensure it is properly fixed. Take the syringe and put it in the adaptor opening (figure 4).





3. Turn the bottle upside down. Fill the syringe with a small amount of syrup by pulling the piston down (figure 5A), then push the piston upwards in order to remove any possible bubble (figure 5B). Pull the piston down to the graduation mark corresponding to the quantity in millilitres (ml) prescribed by your doctor (figure 5C).



4. Turn the bottle the right way up (figure 6A). Remove the syringe from the adaptor (figure 6B).

5. Empty the contents of the syringe into the patient's mouth by pushing the piston to the bottom of the syringe (figure 7). Leave the syringe adaptor in place after first use. Close the bottle with the plastic screw cap. Wash the syringe with water (figure 8).

7. MARKETING AUTHORISATION HOLDER

Syri Limited
Unit 4, Bradfield Road,
Ruislip, Middlesex,
HA4 0NU, UK

Trading as:
Thame Laboratories,
Unit 4, Bradfield Road,
Ruislip, Middlesex,
HA4 0NU, UK

OR

Trading as:
SyriMed,
Unit 4, Bradfield Road,
Ruislip, Middlesex,
HA4 0NU, UK.

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