# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

Alimemazin Orifarm 40 mg/ml, oral drops, solution

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

*1 ml oral drops 40 mg/ml contains:*
Alimemazine hemitartrate corresponding to alimemazine 40 mg.

Excipients with known effect:
1 ml contains: Saccharin sodium 2 mg, propylene glycol 80 microgram and sucrose 160 mg.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Oral drops, solution
Clear, light-yellow solution.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Adults and children from 3 years:
- Premedication.
- Short term treatment of pruritus and allergies.

### 4.2 Posology and method of administration

The dose should be decided individually.
Alimemazine should be used at the lowest effective dose and for the shortest possible treatment time.
The recommended dose should not be exceeded (see also section 4.4).

*Premedication:*
2-4 mg per kg body weight, however maximum 50 mg, at least 2 hours before examination or anaesthesia. A lower dose of alimemazine could preferably be given the evening before. Atropine or equivalent medicinal product should be given, in the usual way, to reduce bronchial secretion.

*Pruritus and allergies:*
Adults: 5 mg 2-4 times daily. Children: 3-5 years: 2.5-10 mg, 5-12 years: 2.5 - 15 mg daily.
The daily dose should be divided into a morning, noon and evening dose, with a larger dose given in the evening.

[Invented name] oral drops can be diluted with a suitable beverage, e.g. juice, lemonade, coffee, but *not* milk, before ingestion.

A drip pipette for dosing [Invented name] oral drops is included in the pack.
The pipette is graduated 0.25 ml, 0.5 ml, 0.75 ml and 1 ml.
One drop with the pipette corresponds to about 1 mg of alimemazine.

| Pipette graduation | Corresponding amount of alimemazine |
|---|---|
| 0,25 ml | 10 mg |
| 0,50 ml | 20 mg |
| 0,75 ml | 30 mg |
| 1 ml | 40 mg |
| Drops | Corresponding amount of alimemazine |
| 1 drop | Approx. 1 mg |

## 4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Leucopenia, also previous agranulocytosis.
- Myastenia gravis.

Alimemazine is contraindicated in children below the age of 3 years (see section 4.4).

## 4.4 Special warnings and precautions for use

Patients are strongly advised to refrain from alcoholic beverages and/or substance use during treatment. Deaths have been reported with concomitant alcohol consumption and/or substance use (see sections 4.5 and 4.9), additional mortality risk has been noted for oral drops.

[Invented name] should be used with caution in patients with hepatic and renal damage, spasticity, epilepsy and seizures, and Parkinson's disease. In more severe cases of extrapyramidal side effects, discontinuation of alimemazine should be considered. The extrapyramidal side effects are treated with a medicinal product for parkinsonism.

[Invented name] is contraindicated in children under 3 years of age due to the risk of a pronounced sedative effect.

[Invented name] should be used with caution in elderly patients, who may be more sensitive to the effects of alimemazine such as extrapyramidal reactions, dizziness, tiredness, fall in blood pressure, urinary retention and constipation.

Alimemazine has anticholinergic effects that can cause urinary retention and should therefore be used with caution by elderly patients with suspected prostate hypertrophy.

[Invented name] should be used with caution in patients with narrow-angle glaucoma.

In randomized, placebo-controlled clinical trials of certain atypical neuroleptics in patients with dementia, the risk of cerebrovascular events was increased by 3 times. The mechanism behind this increase in risk is not known. An increased risk cannot be excluded for other neuroleptics and among other patient populations. Alimemazine should therefore be given with caution in patients with risk factors for stroke.

Paradoxical side effects such as restlessness, difficulty sleeping and euphoria have been reported for phenothiazine derivatives and other antihistamines.

*Skin*
Exposure to sunlight should be avoided during treatment with products belonging to the medicinal group phenothiazines. Increased sensitivity to touch and rash is also associated with the use of phenothiazines.

*QT interval*

Phenothiazines may prolong the QT interval and cause cardiac arrhythmias. Cases of sudden death that may have a cardiac cause have been reported (see sections 4.8, 4.9). Therefore, caution is advised when treating patients with pronounced bradycardia, cardiovascular disease, and with a hereditary form prolongation of the QT interval. Caution is also advised when co-administering other medicinal products that may prolong the QT interval (see sections 4.5, 4.8, 4.9). Concomitant treatment with other neuroleptics should be avoided.

*Neuroleptic malignant syndrome*
Neuroleptic malignant syndrome (NMS) has been reported in connection with overdosing of alimemazine or in combined treatment with alimemazine and a neuroleptic. The symptoms of NMS include a combination of hyperthermia, muscular stiffness, changed mental state and signs of autonomic instability. As this syndrome may be fatal, alimemazine must be discontinued immediately, and intensive clinical follow-up and symptomatic treatment must be started.
Strict compliance with dose recommendations is essential (see also section 4.2).

*Excipients*
This medicinal product contains saccharin sodium and sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
This medicinal product may be harmful to the teeth at long-term use.

## 4.5 Interaction with other medicinal products and other forms of interaction

Caution is advised in concomitant treatment with certain other medicinal products as serious adverse reactions and deaths have been reported (see sections 4.4 and 4.9). The sedative effect of phenothiazines may be increased by alcohol, anti-anxiety drugs, hypnotic drugs, barbiturates, opiates and other sedatives. The anticholinergic effect of phenothiazines may be enhanced by other anticholinergic drugs.

Caution is advised in concomitant treatment with other medicinal products that may prolong the QT interval, such as other neuroleptics, Class IA and III antiarrhythmics, moxifloxacin, erythromycin, methadone, mefloquine, tricyclic antidepressants, lithium and cisapride.

Concomitant use of medicinal products which may cause electrolyte disturbances, for example thiazide diuretics (hypokalaemia), warrant consideration, as this increases the risk of malignant arrhythmias (see also section 4.4, 4.8, 4.9).

The following combinations with alimemazine may require adjustment of the dose:
- Levodopa: Phenothiazine derivatives counteracts the effect of L-dopa through its blockage of the dopamine receptors in the brain.
- Lithium: Cases of reversible neurotoxic syndrome have been described when lithium was co-administered with neuroleptics (particularly haloperidol and thioridazine).
  Symptoms: confusion, desorientation, unconsciousness, fever and extrapyramidal adverse effects.
  Several patients had received very high doses of haloperidol, and at the same time their lithium levels in plasma were unnecessarily high. This was probably due to additive effects of lithium and neuroleptics.
  This syndrome is still described as an interaction in international literature.

## 4.6 Fertility, pregnancy and lactation

*Pregnancy*
High doses of neuroleptics such as chlorpromazine and fluphenazine, given during the last trimester, have caused prolonged but transient neurologic disturbances of extrapyramidal nature in children. Some behaviour disorders, such as learning and motor function disturbances, have been described in studies of rabbits and rats when haloperidol was given during the latter part of the pregnancy. It cannot be excluded that these characteristics can be observed in all substances with a blocking effect on the dopamine receptor. During the last trimester, alimemazine should therefore only be given upon strict indication, and after the needs of the mother have been carefully weighed against the risks  the foetus.

*Breast-feeding*
Alimemazine passes into breast milk. The mother's need for treatment with alimemazine and the benefits of breast-feeding must be weighed against the potential risks to the baby.

*Fertility*
There is no information on the effect of alimemazine tartrate on fertility.

### 4.7 Effects on ability to drive and use machines

During treatment with alimemazine, the ability to react may be reduced. This should be considered when special alertness is required, e.g. when driving or using machines.

### 4.8 Undesirable effects

Treatment with phenothiazines may give rise to a prolongation of the QT interval and cardiac arrhythmias. Cases of sudden death with possible cardiac reasons (see section 4.4) have been reported in treatment with such medicinal products.
Most of the adverse effects are due to the pharmacological effects and are thus dose-dependent. The frequency of the adverse effects varies depending on the dose level, treatment duration and indications.

Adverse effects are listed according to organ class in MedDRA. Within each organ class, the drug-related adverse effects are ranked by frequency, with the most common side effects first. Within each frequency group, the drug-related adverse effects are presented in order of decreasing severity. The corresponding frequency category for each adverse effect is defined as: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

| **Frequency**<br><br>**Organ system** | **Common** | **Uncommon** | **Rare** | **Not known** |
|---|---|---|---|---|
| **Blood and lymphatic system disorders** | | | Agranulocytosis, leucopenia. | |
| **Nervous system disorders** | | | Tardive dyskinesia, parkinsonism, akathisia, acute dystonia. | |
| **Eye disorders** | | Accommodation disorders. | Cloudiness of lens and cornea (high dose/longterm treatment). | |
| **Cardiac disorders** | | | QT-prolongation, Torsade de Pointes, cardiac arrest, ventricular arrhythmias – ventricular fibrillation, ventricular tachycardia, fall in blood pressure, tachycardia. | |
| **Respiratory, thoracic and mediastinal disorders** | Nasal congestion. | | | Respiratory disorders in children. |

| Frequency<br><br>Organ system | Common | Uncommon | Rare | Not known |
|---|---|---|---|---|
| **Gastrointestinal disorders** | Dry mouth. | Constipation. | | |
| **Hepatobiliary disorders** | | | Hepatitis with icterus of stasis type. | |
| **Musculoskeletal and connective tissue disorders** | | | | Seizures. |
| **Renal and urinary disorders** | | Urinary retention. | | |
| **General disorders and administration site conditions** | Tiredness, headache, slight dizziness. | | Neurologic malignant syndrome. | |

In long-term treatment, dry mouth may cause damages on teeth and oral mucous membranes.
Seizures have been reported. Respiratory disorders have been reported in babies during treatment with phenothiazines.

Elderly and volume-reduced patients are particularly at risk for orthostatic hypotension.
Hyperprolactinemia which may lead to galactorrhoea, gynecomastia, amenorrhea and impotence have been reported with drugs in the phenothiazine group.

**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 national reporting system listed in Appendix V.

### 4.9 Overdose

*Toxicity:* 20 mg to a child aged 2.5 years and 40 mg to a child aged 3 years caused mild intoxication. 50-70 mg to a child aged 6 months, 160 mg to a child aged 4 years and 300 mg to a child aged 7 years (after gastric emptying), caused a moderate intoxication. 6 g to an adult caused, after gastric emptying, a moderate to serious intoxication. 0.8-1.2 g and 2 g, respectively, together with alcohol to an adult caused a serious intoxication. Overdose with alimemazine is associated with mortality risk.

Overdose in combination with alcohol, substance use or other drugs is associated with additional mortality risk (see 4.4 and 4.5), additional mortality risk has been noted for oral drops.

*Symptoms:* Causes primarily various degrees of CNS depression, from tiredness, somnolence to deep unconsciousness. Sinus tachycardia may occur, but the effect on the circulation is often small.
Prolonged QT time and cases of serious arrhythmias with fatal outcome have been described after overdoses of phenothiazines.

*Treatment:* If justified, gastric emptying. Repeated doses of charcoal are not of any value. Monitoring of especially the consciousness and respiration.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihistamines for systemic use. Phenothiazine derivatives. ATC code: R06AD01

Alimemazine is a phenothiazine derivative in the group of high-dose neuroleptics with sedative and histamine antagonistic properties. The functions of the autonomic nervous system, circulation and respiration are only affected to a small extent. Alimemazine has an anticholinergic effect. The effects of hypnotics, analgesics and anesthetics are potentiated by alimemazine.

### 5.2 Pharmacokinetic properties

-

### 5.3 Preclinical safety data

-

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Peppermint flavour (contains propylene glycol)
Spearmint flavour
Saccharin sodium
Citric acid, anhydrous (E330)
Macrogolglycerol hydroxystearate
Glycerol
Sucrose
Water

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

30 months

### 6.4 Special precautions for storage

Do not store above 30°C. Keep the bottle in the outer carton in order to protect from light.

### 6.5 Nature and contents of container

Brown glass bottle of 25 ml or 50 ml, with a screw cap in PP/PE (child-resistant). A drip pipette in glass with a cap of PP/TPE for dosing is included in the package (graduated 0.25 ml, 0.50 ml, 0.75 ml and 1 ml).

### 6.6 Special precautions for disposal <and other handling>

The bottle should be closed immediately after use.

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

## 7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

## 8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

## 10. DATE OF REVISION OF THE TEXT

24 July 2024

Detailed information on this medicinal product is available on the website of {name of Member State Agency}