SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Alimemazin Evolan 20 mg capsule, hard

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains alimemazine hemitartrate corresponding to alimemazine 20 mg.

Excipients with known effect: Each capsule contains 59.5 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule, hard.

White, cylindrical gelatin capsule, length 14.3 ± 0.3 mm

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Premedication.
Short-term treatment of sleep disorders in adults.

4.2 Posology and method of administration

Posology
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 in adults and children over 12 years: 2-4 mg per kg body weight, however maximum 50 mg at least 2 hours before examination or anesthesia. A smaller dose of alimemazine could preferably be given the evening before. Atropine or equivalent medicinal product should be given, in the usual way, to reduce the bronchial secretion.
Other pharmaceutical forms such as alimemazine in the form of oral drops, solution are available for children 3-12 years.

Short-term treatment of sleep disorders in adults: 10-30 mg 1-2 hours before bedtime. At doses other than 20 mg, another alimemazine-containing product should be selected.

Pediatric population
Alimemazin Evolan is not recommended in children below the age of 3 years (see section 4.3).

Method of administration
The capsules should be swallowed whole together with water.

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.

4.4 Special warnings and precautions for use

Patients are strongly advised to refrain from consuming alcoholic beverages and/or substance use during treatment. Deaths have been reported with concomitant alcohol consumption and/or substance use (see section 4.5 and 4.9).

Alimemazin Evolan 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.

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Alimemazine should be used with caution by 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.

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

Alimemazine Evolan 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 background mechanistic explanation to this increase in risk is not known. This increased risk can not 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 phentiazines. 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 a hereditary form of 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 an intensive clinical follow-up and symptomatic treatment must be started.
A strict compliance with the recommended dose should be considered (see also section 4.2).

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Caution is advised in concomitant treatment with other medicinal products as serious adverse reactions and deaths have been reported (see sections 4.4 and 4.9). The sedative effect of phentiazines may be increased by alcohol, anti-anxiety drugs, hypnotic drugs, barbiturates, opiates and other sedatives. The anticholinergic effect of phentiazines 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 medication with medicinal products may give rise to electrolyte disorders, for example thiazide diuretics (hypokalaemia). This should be considered, 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 has been combined with neuroleptics (particularly haloperidol and thioridazine). Symptoms: confusion, desorientation, unconsciousness, fever and extrapyramidal adverse effects. Several of these cases had received very high doses of haloperidol, at the same time as the lithium levels in plasma were unnecessarily high. This may probably be due to additive effects of lithium and neuroleptics. This syndrome has still been described as an interaction in the international literature.

4.6 Fertility, pregnancy and lactation

Pregnancy
High doses, given during the last trimester, of neuroleptics such as chlorpromazine and fluphenazine have given rise to prolonged but transient neurologic disturbances of extrapyramidal nature in children. Some behavior disorders, such as the learning and motor function, have been described in studies of rabbits and rats with haloperidol 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 of the foetus.

Breast-feeding
Alimemazine passes into breast milk. The mother's need for treatment with Alimemazine Evolan 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.

In the below table, the adverse effects are listed after classification and frequency:
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)

Organ system	**Frequency**	**Adverse reaction**
Blood and lymphatic system disorders	Rare	Agranulocytosis, leucopenia
Nervous system disorders	Rare	Tardive dyskinesia, parkinsonism, akathisia, acute dystonia
Eye disorders	Uncommon	Accommodation disorders
	Rare	Cloudiness of lens and cornea (high dose/longterm treatment).
Cardiac disorders	Rare	QT-prolongation, Torsade de Pointes, cardiac arrest, ventricular arrhythmias – ventricular fibrillation, ventricular tachycardia, fall in blood pressure, tachycardia.
Respiratory, thoracic and mediastinal disorders	Common	Nasal congestion
Gastrointestinal disorders	Common	Dry mouth
	Uncommon	Constipation
Hepatobiliary disorders	Rare	Hepatitis with icterus of stasis type
Renal and urinary disorders	Uncommon	Urinary retention
General disorders	Common	Tiredness, headache, slight dizziness.
	Rare	Neurologic malignant syndrome

In longterm 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
[to be nationally completed]

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).

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: Neuroleptic with unspecific sedative and antiallergic effect. 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

Information about blood levels, distribution and excretion in humans is poor.

5.3 Preclinical safety data

There are no preclinical data of relevance for the assessment of the safety, besides what has already been described in the summary of product characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Cornstarch
Microcrystalline cellulose
Silica, colloidal anhydrous
Magnesium stearate

Gelatin capsule, hard
Titanium dioxide (E171)
Gelatin

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

A white HDPE-bottle with a LDPE lid, 100, 120 or 200 capsules.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Evolan Pharma AB
P.O. Box 120
SE-182 12 Danderyd, Sweden

8. MARKETING AUTHORISATION NUMBER

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation

10. DATE OF REVISION OF THE TEXT

2024-10-02