SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
OXACATIN

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
oxomemazine.....……..1.65 mg/5 ml
potassium guaiacol sulphonate…..33.3 mg/5 ml

Excipients with known effect: sugar, sorbitol, propylene glycol, sodium benzoate and sodium.
For the complete list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Syrup

4. CLINICAL DATA

4.1. Therapeutic indications
Antitussive expectorant

4.2. Dosage and method of administration

Dosage
RESERVED FOR ADULTS AND CHILDREN OVER 2 YEARS OLD.
In adults: 10 ml per dose, 4 times a day.
Paediatric population
In children: the daily dosage depends on the weight of the child (1 ml of syrup per kg of body weight per day), or as a general guide :
- Children from 13 to 20 kg (2 to 6 years): 5 ml per dose, 2 to 3 times a day,
- Children from 20 to 30 kg (6 to 10 years): 10 ml per dose, 2 to 3 times a day,
- Children from 30 to 40 kg (10 to 12 years): 10 ml per dose, 3 to 4 times a day
- Children over 40 kg (12 years): 10 ml per dose, 4 times a day.

The sockets are to be renewed if necessary and spaced at least 4 hours apart.

Method of administration
Oral. Use the measuring cup.
Vesperal intake should be preferred because of the sedative effect of oxomemazine, especially at the beginning of treatment.

4.3. Contraindications
This medication is CONTRAINDICATED in the following cases:
- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1,
- Hypersensitivity to antihistamines,
- Due to the presence of oxomemazine
  - infant (less than 2 years of age) (see section 4.4),
  - history of agranulocytosis,
  - risk of urinary retention related to urethro-prostate disorders,
  - risk of narrow angle glaucoma,
- In combination with cabergoline or quinagolide (see section 4.5).

4.4. Special warnings and precautions for use

Special warnings:

Productive coughs, which are a fundamental element of bronchopulmonary defense, should be allowed to occur unimpeded.

Before prescribing cough treatment, it is worth looking for the causes of cough that require specific treatment.

If the cough is resistant to cough suppressant given at a usual dosage, there should be no increase in doses, but a review of the clinical situation.

Precautions for use:

Related to the presence of oxomemazine:

Since phenothiazines have been considered hypothetical risk factors for the occurrence of sudden infant death, oxomemazine should not be used in children under 2 years of age.

Monitoring (clinical and possibly electrical) should be strengthened in epileptics due to the possibility of lowering the epileptogenic threshold.

The risk of abuse and drug dependence is low. However, cases of abuse and drug dependence have been reported mainly in adults following misuse of oxomemazine for sedative purposes. The occurrence of signs or symptoms suggestive of abuse or dependence on oxomemazine should be carefully monitored.

Oxomemazine should be used with caution:

- In the elderly with:
  - greater sensitivity to orthostatic hypotension, dizziness and sedation,
  - chronic constipation (risk of paralytic ileus),
  - possible prostatic hypertrophy.
- In subjects with certain cardiovascular conditions, because phenothiazines may cause tachycardia and hypertension In case of severe hepatic and/or renal impairment (due to the risk of accumulation).

When used in children, bronchial asthma or gastroesophageal reflux disease should be eliminated before using oxomemazine as a cough suppressant.

Taking alcoholic beverages or alcohol-containing medicinal products (see section 4.5) is strongly discouraged for the duration of treatment.

Given the photosensitizing effect of phenothiazines, it is better not to expose yourself to the sun during treatment.

H1 antihistamines should be used with caution due to the risk of sedation. Combination with other sedative medicinal products should be discouraged (see section 4.5).

This medicine contains **sorbitol**. Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product.

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

This medicine contains 250 mg **propylene glycol** in each dose of 5 ml. Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce adverse effects in children less than 5 years old.
While propylene glycol has not been shown to cause reproductive or developmental toxicity in animals or humans, it may reach the fetus and was found in milk. As a consequence, administration of propylene glycol to pregnant or lactating patients should be considered on a case.
Medical monitoring is required in patients with impaired renal or hepatic functions because various adverse events attributed to propylene glycol have been reported such as renal dysfunction (acute tubular necrosis), acute renal failure and liver dysfunction.

This medicine contains 33.3 mg of sodium benzoate in each dose of 5 ml, which is equivalent to 0.7% w/w.
This medicine contains less than 1 mmol (23 mg) of sodium per 5 ml dose, i.e. it is essentially "sodium-free".

4.5. Interactions with other medicinal products and other forms of interactions

Drugs that lower the seizure threshold
The joint use of proconvulsant drugs, or lowering the seizure threshold, will have to be carefully weighed, due to the severity of the risk involved. These drugs are represented in particular by most antidepressants (imipramins, selective serotonin reuptake inhibitors), neuroleptics (phenothiazines and butyrophenones), mefloquine, chloroquine, bupropion, tramadol.

Atropinic drugs
It must be taken into account that atropinic substances can add up their adverse effects and more easily lead to urinary retention, an acute flare-up of glaucoma, constipation, dry mouth, etc.
The various atropinic drugs are represented by imipraminic antidepressants, most atropinic H1 antihistamines, anticholinergic antiparkinsonians, atropinic antispasmodics, disopyramide, phenothiazine neuroleptics as well as clozapine.

Sedative drugs
It should be taken into account that many drugs or substances can add their depressant effects of the central nervous system and contribute to decreased alertness. These are morphine derivatives (analgesics, cough suppressants and substitution treatments), neuroleptics, barbiturates, benzodiazepines, anxiolytics other than benzodiazepines (e.g. meprobamate), hypnotics, sedative antidepressants (amitriptyline, doxepin, mianserin, mirtazapine, trimipramine), H1 sedative antihistamines, central antihypertensives, baclofen and thalidomide.

Contraindicated combinations
- Dopaminergics, excluding Parkinson's (cabergoline, quinagolide): Reciprocal antagonism of dopaminergic agonist and neuroleptics.

Combinations that are not recommended
- Other sedative drugs: Potentiation of the sedative effect of H1 antihistamines.
- Alcohol consumption: Increased by alcohol in the sedative effect of these substances. Impaired alertness can make it dangerous to drive vehicles and use machines. Avoid taking alcoholic beverages and alcohol-containing medications.

Combinations requiring precautions for use

- Gastrointestinal agents, antacids and charcoal: Reduction in the intestinal absorption of phenothiazine neuroleptics. Take gastrointestinal agents and antacids away from phenothiazine neuroleptics (more than 2 hours, if possible).

Combinations that need to be considered

- Antihypertensives: Increased risk of hypotension, especially orthostatic hypotension.
- Beta-blockers (except esmolol and sotalol): Vasodilator effect and risk of hypotension, especially orthostatic hypotension (additive effect).
- Beta-blockers in heart failure (bisoprolol, carvedilol, metoprolol, nebivolol): vasodilator effect and risk of hypotension, especially orthostatic hypotension (additive effect).
- Nitrated and related derivatives: Increased risk of hypotension, especially orthostatic.

4.6. Fertility, pregnancy and lactation

The presence of oxomemazine determines the course of action during pregnancy and lactation.

Pregnancy

Malformative aspect:

There are no reliable data on teratogenesis in animals.
There are currently no sufficiently relevant data to assess a possible malformative or fetotoxic effect of oxomemazine when administered during pregnancy.

Fetotoxic aspect:

In newborns of mothers treated over the long term with high dosages of anticholinergic drugs have rarely been described digestive signs related to atropinic properties (abdominal distension, meconial ileus, delay in the emission of meconium, difficulty in starting the diet, tachycardias, neurological disorders ...).
Given these data, the use of this drug is not recommended during the first trimester of pregnancy. It will be prescribed only if necessary thereafter, limited to the 3rd trimester, to a punctual use.
If the administration of this drug took place in late pregnancy, it seems justified to observe a period of monitoring of the neurological and digestive functions of the newborn.

Breastfeeding

It is not known whether oxomemazine is excreted in breast milk. Given the possibilities of sedation or paradoxical excitation of the newborn, and even more so the risks of sleep apnea evoked with phenothiazines, this drug is not recommended in case of breastfeeding.

4.7. Effects on the ability to drive and use machines

For drivers and machine operators in particular, attention should be drawn to the risks of drowsiness linked to the use of this medicinal product, especially at the start of treatment. This phenomenon is accentuated by the intake of alcoholic beverages or drugs containing alcohol.

4.8. Adverse reactions

The pharmacological characteristics of the oxomemazine molecule cause adverse

reactions of unequal intensity and whether dose-related or not (see section 5.1):

Autonomic effects:
- sedation or drowsiness, more marked at the beginning of treatment;
- anticholinergic effects with type of dryness of the mucous membranes, constipation, accommodation disorders, mydriasis, palpitations, risk of urinary retention;
- orthostatic hypotension;
- balance disorders, dizziness, decreased memory or concentration (more common in the elderly);
- motor incoordination, tremors;
- mental confusion, hallucinations;
- more rarely, effects with type of excitement: agitation, nervousness, insomnia.

Psychiatric disorders:
- Abuse/drug dependence (see section 4.4) (frequency not known).

Sensitization reactions:
- erythema, eczema, pruritus, purpura, possibly giant urticaria,
- edema, more rarely angioedema,
- anaphylactic shock
- photosensitization.

Hematological and lymphatic system disorders:
- leukopenia, neutropenia, rarely agranulocytosis,
- hemolytic anemia,
- eosinophilia (frequency not known),
- thrombocytopenia including thrombocytopenic purpura (frequency not known).

Reporting suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continuous monitoring of the benefit/risk balance of the drug. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il.

4.9. Overdose
Signs of oxomemazine overdose: convulsions (especially in children), impaired consciousness, coma.
Symptomatic treatment should be initiated in a specialist setting.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Oxomemazine
Pharmacotherapeutic group: antihistamines for systemic use. ATC code: R06AD08
Antihistamine H1, phenothiazine with aliphatic side chain, which is characterized by:
- a marked sedative effect at the usual doses, of histaminergic and central adrenolytic origin,
- an anticholinergic effect causing peripheral side effects,
- a peripheral adrenolytic effect, which can resonate at the hemodynamic level (risk of orthostatic hypotension).

Antihistamines have in common the property of opposing, by competitive antagonism more or less reversible, the effects of histamine especially on the skin, bronchi, intestine, and vessels.

Potassium guaiacol sulphonate:
Pharmacotherapeutic group: expectorant. ATC code R05CA09.

5.2. Pharmacokinetic properties

Pharmacokinetic data with oxomemazine are lacking.
For all antihistamines, including phenothiazines, general elements can be provided:

- Bioavailability is generally average.
- If necessary, the metabolism can be intense, with the formation of many metabolites, which explains the very small percentage of product found unchanged in the urine.
- The half-life is variable but often prolonged, allowing a single daily intake.
- The fat solubility of these molecules is at the origin of the high value of the volume of distribution.

Pathophysiological variation: risk of accumulation of antihistamines in patients with renal or hepatic impairment.

5.3. Preclinical safety data

Not applicable

6. PHARMACEUTICAL DATA

6.1. List of excipients

Sugar, sorbitol 70% solution, propylene glycol, sodium benzoate, sodium citrate, caramel flavor, citric acid anhydrous, caramel color liquid, purified water.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

The expiry date is indicated on the printing materials.
Store for a maximum of 12 months after the first opening of the bottle.

6.4. Special storage precautions

Store below 25°C.
For storage conditions of the medicinal product after first opening, see section 6.3.

6.5. Nature and contents of the outer packaging

30 ml in bottle (amber polyethylene terephthalate) with child safety closure and measuring cup (polypropylene).
120 ml in bottle (amber polyethylene terephthalate) with child safety closure and measuring cup (polypropylene).
Not all presentations may be marketed.

6.6. Special disposal and handling precautions

No special requirements for disposal.
Any unused medication or waste must be disposed of in accordance with current regulations.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURER
Taro Pharmaceutical Industries Ltd., 14 Hakitor St., Haifa Bay 2624761

8. MARKETING AUTHORISATION NUMBER
030-54-21959-00

Revised in May 2024 according to MOH guidelines.