PART I B

SUMMARY
OF
PRODUCT CHARACTERISTICS

ALLERGOVET®

10% injectable solution
1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ALLERGOVET® 10% injectable solution.

1.1. NOMENCLATURE OF THE ACTIVE SUBSTANCE

DIPHENHYDRAMINE HYDROCHLORIDE

Name of the active substance:
Diphenhydramine hydrochloride.

International non-proprietary name (INN):
Diphenhydramine hydrochloride.

European Pharmacopoeia:
Included in Eur. Ph., 4th Ed.

Other names:

Chemical Abstracts Name:
2-Diphenylmethoxy-N,N-di-methylethanamine;
Alternate chemical names:

2-(benzhydryloxy)-N,N-dimethylethyl-amine;
β-dimethylaminoethyl benzhydryl ether]
O-benzhydryldimethyaminoethanol;
β-dimethylaminoethanol diphenylmethyl ether;
α-(2-dimethylaminoethoxy)diphenylmethane;
benzhydramine.

CAS Registry Number:

[147-24-0].

Therapeutic classification:

Antihistaminic.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION OF THE PRODUCT

<table>
<thead>
<tr>
<th>NAME OF INGREDIENTS</th>
<th>CONTENT</th>
<th>FUNCTION</th>
<th>REFERENCE TO STANDARD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphenhydramine hydrochloride</td>
<td>0,1 g</td>
<td>active substance</td>
<td>Eur.Ph.</td>
</tr>
<tr>
<td>Water for injections</td>
<td>up to 1,0 ml</td>
<td>solvent</td>
<td>Eur.Ph</td>
</tr>
</tbody>
</table>
3. **PHARMACEUTICAL FORM**

Injectable solution.

4. **PHARMACOLOGICAL PROPERTIES**

4.1. **SHORT DESCRIPTION OF THE ACTIVE INGREDIENT**

Diphenhydramine hydrochloride is an antihistaminic agent, blocking the H<sub>1</sub>-histamine receptors. It removes the effects obtained as a result of the increased histamine content in blood and tissues, respectively its action on blood and smooth muscles. It induces almost no effect on the secretory function of the gastric glands. It has a local anaesthetic, sedative, ganglioplegic, antiinflammatory and antitussive action.

**Structural formula:**

![Structural formula image]

**Molecular formula:**

C<sub>17</sub>H<sub>22</sub>CINO
Molecular mass:
291.8

4.2. PHARMACODYNAMIC PROPERTIES

Antihistamines are reversible, competitive inhibitors of the most of the pharmacological actions of histamines. One exception is the stimulation of gastric acid secretion, which is mediated by H₂-receptors. Most antihistamined do not chemically inactivate or physiologically antagonize histamine, nor do they prevent histamine release. Actions of histamine inhibited by H₁-antagonists include constriction of respiratory smooth muscle, increased capillary permeability, and edema and wheal formation. Since the basic ethylamine group common to antihistamines is also common to anticholinergics, ganglionic- and adrenergic-blocking agents, local anaesthetics, and antispasmodics, some antihistamines may exhibit some of the activities of these other classes of drugs. H₁-receptor antagonists induce and may facilitate their own metabolism.

Antihistamines act as competitive antagonists for specific histamine receptors in the tissue cells; their binding to the cell receptors evokes no direct cellular action. This mechanism of action is based on quantitative considerations; therefore, histamine in excess may displace antihistamines. Generally, antihistamines are more effective against exogenously administered histamine that against endogenously released histamine. They are also more effective in preventing actions of histamine than in reversing them.
4.3. PHARMACOKINETIC PROPERTIES

Diphenhydramine is absorbed satisfactorily after peroral administration in monogastric animals but not in ruminants. Effects are usually expected within 20-45 min after oral administration, and the duration of action ranges from 3 to 12 hours.

Diphenhydramine undergoes first-pass metabolism in the liver, and only 40% to 60% of the dose reaches the systemic circulation as unchanged drug.

After intravenous administration of diphenhydramine in rats, the highest concentrations are attained in lungs, spleen and brain, with lower concentrations in the heart, muscle and liver. Peak plasma concentrations of ethanolamine-derivative antihistamines to the class of which diphenhydramine belongs, are reached within 1 to 5 hours and elimination half-life varies from 2.4 to 10 hours.

5. CLINICAL PARTICULARS

5.1. TARGET ANIMAL SPECIES

Single-hoofed animals (equine species), large and small ruminants, pigs, dogs.
5.2. **INDICATIONS**

Allergies, anaphylactic and inflammatory diseases - urticaria, allergic dermatides and dermatoses, allergic conjunctivitis, drug and feed related allergies, anaphylactic shock; aseptic total (diffuse) pododermatitis (laminitis acuta), periodic ophthalmia and chronic alveolar emphysema in horses; bronchial asthma, atony of forestomach and retained placenta in large and small ruminants; gangrenous mastitis in sheep; oedema disease in piglets; cases of insect and snake bites; transport disease; for anaesthesia of the nasal mucosa.

5.3. **CONTRAINDICATIONS**

In cases of hypersensitivity to antihistamine drugs belonging to the group of monoethanolamine; not to be applied during allergic diagnostic tests (tuberculinization, maleinization, etc.) - the administration must be stopped at least 4 days prior to the test; in glaucoma.

5.4. **SIDE EFFECTS**

Sedative effect which could decrease the efficiency of working dogs (hunting dogs, guarding dogs, etc.).

5.5. **SPECIAL PRECAUTIONS AND WARNINGS**

Not envisaged.
5.6. **USE DURING PREGNANCY AND LACTATION**

Not contraindicated for pregnant and lactating animals.

5.7. **MEDICINAL AND OTHER INTERACTIONS**

When administered simultaneously with narcotic drugs and tranquilizers, diphenhydramine could reinforce the effect they induce on the central nervous system. The effect of diphenhydramine is enhanced by MAO-inhibitors. It could reduce the anticoagulant effect of heparin and warfarin. It reduces the effect of steroids.

5.8. **MODE OF ADMINISTRATION**

Intramuscular, subcutaneous, external.

5.9. **DOSAGE**

*Parenterally:*
Average doses - 1 - 2 mg/kg b.w.
Single doses of the preparation - parenterally:
- Large ruminants - 3.0 - 6.0 ml;
- Horses - 1.0 - 5.0 ml;
- Small ruminants - 0.5 - 0.8 ml;
- Pigs - 0.5 - 0.7 ml;
• Dogs - 0.1 - 0.4 ml.

Note:
In shock conditions the dosage levels may be duplicated.

Topically:
For anaesthesia of the mucosa use the 10% solution on drops.

5.10. OVERDOSAGE

If overdosaged or when administered for a continuous period of time in carnivora, excitation or depression, vomiting, diarrhea and loss of appetite could be observed, and in the more severe cases - respiratory depression, coma and death. The affected animals must be treated with symptomatic drugs.

5.11. SPECIAL PRECAUTIONS FOR THE TARGET SPECIES

Not envisaged.

5.12. WITHDRAWAL PERIODS

No withdrawal period is recommended.

5.13. SPECIAL PRECAUTIONS WHILE HANDLING THE PRODUCT

Not envisaged.
6. PHARMACEUTICAL PARTICULARS

6.1. INCOMPATIBILITIES

In solutions diphenhydramine is compatible with almost every medicinal products - amikacin, aminophylline, ascorbic acid, atropine, erythromycin, lidocaine, penicillin, polymyxin B, tetracycline, B-complex vitamins, etc. It is incompatible with barbiturates, amphotericin B, cephalothin, hydrocortisone.

6.2. SHELF-LIFE

3 (three) years from the manufacture date.

6.3. STORAGE CONDITIONS

In original market containers at temperature (15-25) °C in dry premises protected from direct sunlight.

6.4. PACK TYPE AND SIZE

Allergovet 10% injectable solution is packed in glass vials closed with rubber stoppers.

Two pack sizes are available: 25 ml and 50 ml.
6.6. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS

Dispose of unused products and containers by incineration.

7. FINAL INFORMATION

7.1. LEGAL CATEGORY OF THE PRODUCT

Prescription only medicine (POM).

7.2. MANUFACTURER

BIOVET Joint Stock Company
39, Petar Rakov Street
Peshtera 4550, Bulgaria