

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Belavit AD<sub>3</sub>E, solution for injection for horses, cattle, pigs, and dogs

### **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

1 ml solution for injection contains:

#### **Active substance:**

Retinol palmitate (equivalent to 300,000 I.U. Vitamin A)	176.47 mg
all-rac alpha tocopheryl acetate (equivalent to 45.56 mg alpha-tocopherol) (Vitamin E)	50.00 mg
Oily solution of cholecalciferol (contains 2.5 mg cholecalciferol; equivalent to 100,000 I.U. Vitamin D <sub>3</sub> )	100.00 mg

For the full list of excipients, see section 6.1.

### **3. PHARMACEUTICAL FORM**

Solution for injection  
Clear, yellow solution

### **4. CLINICAL PARTICULARS**

#### **4.1 Target species**

Cattle, horses, pigs and dogs.

#### **4.2 Indications for use, specifying the target species**

Treatment of combined vitamin A, vitamin D, and vitamin E deficiencies.

#### **4.3 Contraindications**

Do not use in food producing animals with adequate vitamin A supply due to the possibility of accumulation in edible tissues.

The treatment with Vitamin AD<sub>3</sub>E is contraindicated in case of a hypervitaminosis.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

#### **4.4 Special warnings for each target species**

None.

#### **4.5 Special precautions for use**

##### Special precautions for use in animals

The recommended dose and duration of treatment should not be exceeded. The use of intramuscular lipid-soluble vitamin products in horses may increase the risk of myositis and myonecrosis.

##### Special precautions to be taken by the person administering the veterinary medicinal product to animals

- In case of accidental self-injection, a risk of hypervitaminosis in relation to vitamin A cannot be excluded. Therefore, administration should be performed with great caution. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
- Studies with vitamin A in laboratory animals have shown evidence of teratogenic effects. Therefore, this product should not be administered by pregnant women.
- This product may cause irritation of eyes and skin. Contact with eyes and skin should be avoided and any accidental spillage onto the eyes or skin should be rinsed off with water immediately.
- This product may cause hypersensitivity (allergic) reactions in sensitised people. People with known hypersensitivity to any of the active substances should avoid contact with the product. If you develop symptoms such as a rash after accidental exposure, seek medical advice and show the physician this warning. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.
- Wash hands after use.

#### **4.6 Adverse reactions (frequency and seriousness)**

A temporary swelling at the injection site may occur. In rare cases anaphylactic reactions may be observed.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

#### **4.7 Use during pregnancy, lactation or lay**

There are indications of teratogenic effects of high doses of vitamin A in humans and laboratory animals. The safety of the veterinary medicinal product has not been established during pregnancy and lactation in the target species. Therefore, use only according to the benefit/risk assessment by the responsible veterinarian.

#### **4.8 Interaction with other medicinal products and other forms of interaction**

None known.

#### **4.9 Amounts to be administered and administration route**

This veterinary medicinal product should not be used by subcutaneous route of administration in food producing species.

For intramuscular use in horses, cattle and pigs.  
For subcutaneous or intramuscular use in dogs.

Vitamin AD<sub>3</sub>E pro injectione as a single injection per animal:

Cattle: 5 ml  
Horse: 2 – 4 ml  
Calf: 2 ml  
Pig: 1 ml  
Weaned piglet: 0.2 – 0.4 ml  
Piglet: 0.1 – 0.2 ml  
Dog: 0.05 – 0.3 ml

The proposed injection volumes correspond to the following concentrations of vitamins:

Target animal species	Injection volume	Vitamin A	Vitamin D <sub>3</sub>	Vitamin E
Horse (500 kg)	2.5 ml	1500 IU/kg bw	500 IU/kg bw	0.25 mg/kg bw
Cattle (500 kg)	5 ml	3000 IU/kg bw	1000 IU/kg bw	0.5 mg/kg bw
Calf (100 kg)	2 ml	6000 IU/kg bw	2000 IU/kg bw	1.0 mg/kg bw
Pig (100 kg)	1 ml	3000 IU/kg bw	1000 IU/kg bw	0.5 mg/kg bw
Weaned piglet (40 kg)	0.4 ml	3000 IU/kg bw	1000 IU/kg bw	0.5 mg/kg bw
Piglet (10 kg)	0.1 ml	3000 IU/kg bw	1000 IU/kg bw	0.5 mg/kg bw
Dog (30 kg)	0.2 ml	2000 IU/kg bw	667 IU/kg bw	0.33 mg/kg bw

For single administration.  
The stopper could be punctured up to 50 times.

**4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary**

A substantial overdose of vitamin A is related to the risk of intoxication (hypervitaminosis). Symptoms of acute vitamin A intoxication include somnolence, motoric disorders, vomiting, and squamous skin degeneration. Following an overdose in pregnant animals, especially in the early stage of gestation, an increase number of foetal absorption, stillbirths and malformations may be observed.

The main effect of a vitamin D hypervitaminosis is hypercalcaemia with associated symptoms including organ calcification and renal and cardiovascular damage.

**4.11 Withdrawal period(s)**

Cattle: meat and offal: 259 days  
milk: 120 hours (5 days)  
Horse: meat and offal: 250 days

Not authorised for use in horses producing milk for human consumption.

Pig: meat and offal: 194 days

## **5. PHARMACOLOGICAL PROPERTIES**

Pharmacotherapeutic group: vitamin combination

ATC vet code: QA11JA

### **5.1 Pharmacodynamic properties**

#### **Vitamin A (Retinol)**

As a fat-soluble vitamin, vitamin A belongs to those vitamins, which affect - like steroid hormones - gene expression. In consequence it is essential for growth, for cell differentiation, reproduction of males and female animals and human being, for vision, for bone development and for the immune response.

Both deficiency and excess may cause severe dysfunctions of these processes in man and animal. Vitamin A homeostasis in plasma is tightly controlled. Abnormal plasma levels may therefore only be detected in case of extreme high or extreme low vitamin A availability. Liver biopsy may provide more sensible information on the vitamin A status of an animal.

The liver is of central importance in vitamin A metabolism and serves as the major vitamin A reservoir.

#### **Vitamin D<sub>3</sub> (Cholecalciferol)**

As a fat-soluble vitamin, vitamin D belongs to those vitamins, which affect - like steroid hormones - gene expression. Vitamin D is essential for regulation of calcium metabolism. In most animal species, especially in poultry, Vitamin D<sub>3</sub> possesses a stronger activity than vitamin D<sub>2</sub> (ergocalciferol).

#### **Vitamin E (α-Tocopherol)**

Vitamin E belongs to the group of fat-soluble vitamins. The tocopherols are important physiological antioxidants. Vitamin E protects the unsaturated fatty acids (e.g. lipids of the cytoplasmic and mitochondrial membranes) against oxidation.

Besides its importance as antioxidant, vitamin E stimulates the formation of prostaglandin E from arachidonic acid and hinders blood coagulation. In its protective function for leucocytes and macrophages, it ensures phagocytosis and stimulates the immune response.

Deficiency of vitamin E may cause nutritional diseases as muscle dystrophy, exudative diathesis, encephalomalacia, and liver necrosis.

An excess of unsaturated fatty acids supports vitamin E deficiency symptoms.

### **5.2 Pharmacokinetic particulars**

#### **Vitamin A**

Following a single parenteral administration of  $1 \times 10^6$  I.U. in cattle, an increase in vitamin A plasma values is observed. In animals provided sufficiently with vitamin A

within 2 days, the plasma values increase from  $160 \pm 37$  to  $8641 \pm 1593$   $\mu\text{g/l}$  and return within 8 days to their basic values. Vitamin A is transported to the liver, where it is stored. Excretion occurs in form of the glucuronide with the bile. In the small intestines the molecule is de-glucuronidated and vitamin A is absorbed once again (enterohepatic circulation). A fraction of vitamin A is excreted with the urine.

### **Vitamin D<sub>3</sub> (Cholecalciferol)**

Vitamin D<sub>3</sub> is transported via the lymph to the liver, where it is hydroxylated in the biologically active hydroxy compounds. In the kidneys 1,25- and 24,25 Dihydroxyvitamin D<sub>3</sub> are formed. 1,25-Dihydroxy-Vitamin D<sub>3</sub> (Calcitriol) shows the highest biological efficacy.

### **Vitamin E ( $\alpha$ -Tocopherol)**

Following parenteral administration vitamin E is distributed via the lymph into systemic circulation and peak plasma levels are obtained after 4 to 9 hours. In the blood vitamin E is mainly bound to  $\beta$ -lipo-proteins. Vitamin E accumulates in the liver, cardiac muscle, in fat tissue and the adrenal gland. The majority of vitamin E is excreted by the liver with the bile, the remaining with the urine.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Medium-chain triglycerides  
DL-alpha-tocopherol (E307)

### **6.2 Major incompatibilities**

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

### **6.3 Shelf life**

Shelf life of the veterinary medicinal product as packaged for sale: 2 years  
Shelf life after first opening the immediate packaging: 28 days

### **6.4 Special precautions for storage**

Do not store above 30 °C.

### **6.5 Nature and composition of immediate packaging**

100 ml brown glass type II vials with bromobutyl stoppers and aluminium caps, packed in carton boxes of 1, 6 or 12 vials.

1 x 100 ml  
6 x 100 ml  
12 x 100 ml

Not all pack sizes may be marketed.

**6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products**

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

**7. MARKETING AUTHORISATION HOLDER**

bela-pharm GmbH & Co. KG  
Lohner Str. 19  
49377 Vechta  
Germany

**8. MARKETING AUTHORISATION NUMBER**

Vm 41816/4004

**9. DATE OF FIRST AUTHORISATION**

12 July 2019

**10. DATE OF REVISION OF THE TEXT**

December 2021

Approved: 23/12/21

