

**IRISH MEDICINES BOARD ACT 1995, as amended**

**European Communities (Animal Remedies) (No. 2) Regulations 2007**

VPA: **10988/066/001**  
Case No: 7004829

The Irish Medicines Board in exercise of the powers conferred on it by Animal Remedies (No. 2) Regulations (S.I. No. 786 of 2007) hereby grants to:

**Virbac S.A.**

**Virbac 1, 1 ere Avenue, 2065 M - L.I.D., BP 27, 06516, Carros Cedex, France**

an authorisation, subject to the provisions of the said Regulations and the general conditions of the attached authorisation, in respect of the Veterinary Medicinal Product:

**Alizin 30mg/ml Solution for injection**

The particulars of which are set out in the attached Schedule. The authorisation is also subject to any special conditions as may be specified in the Schedule.

The authorisation, unless revoked, shall continue in force from **26/11/2008**.

Signed on behalf of the Irish Medicines Board

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A person authorised in that behalf by the said Board.

(NOTE: This authorisation replaces any previous authorisation in respect of this product which is now null and void.)

## Part II

### Summary of Product Characteristics

#### 1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Alizin 30mg/ml Solution for Injection.

#### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml contains:

##### **Active substance**

Aglepristone 30 mg

For a full list of excipients, see section 6.1

#### 3 PHARMACEUTICAL FORM

Solution for injection.

Clear, yellow oily solution.

#### 4 CLINICAL PARTICULARS

##### 4.1 Target Species

Dogs (bitches).

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

Pregnant bitches: induction of abortion up to 45 days after mating.

##### 4.3 Contraindications

Do not use in dogs with impaired hepatic or renal function, in diabetic animals or in dogs in poor health.

Do not use in dogs with either manifest or latent hypoadrenocorticism (Addison's disease) or in dogs with a genetic predisposition to hypoadrenocorticism.

Do not use in dogs with known hypersensitivity to aglepristone or the veterinary medicinal product excipient.

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

Rare cases of lack of efficacy (>0.01 % to < 0.1%) have been reported as part of the pharmacovigilance survey. To reduce the possibility of lack of expected efficacy, avoid the use of Alizin until after the end of oestrus and avoid new mating before the end of oestrus.

In bitches confirmed pregnant, a partial abortion was observed in 5% of cases in field trials. A thorough clinical examination is always recommended in order to confirm that the uterus content is fully evacuated. Ideally, the examination should be conducted using ultrasound. This examination should be performed 10 days after treatment and at least 30 days after mating.

In case of partial abortion or no abortion, repeat treatment may be recommended 10 days after treatment, between day 30 and day 45 after mating. Surgery should also be considered..

## 4.5 Special precautions for use

### (i) Special precautions for use in animals

In the absence of available data, the veterinary medicinal product should be used with caution in dogs with chronic obstructive-airway disease and/or cardiovascular disease, particularly bacterial endocarditis.

Fatalities have been reported subsequent to off-label use in seriously ill bitches with uterine infections. A causal association is difficult to determine but is unlikely.

In up to 50 % of bitches, mating may not be followed by pregnancy. The possibility that a bitch may therefore be treated unnecessarily should be taken into account in evaluating the product risk-benefit ratio.

Bitches that remain pregnant despite treatment should be monitored, as viability of the puppies may be compromised.

Possible long-term effects of treatment have not been studied.

Owners should be advised to consult their veterinary surgeon if their dog shows the following signs after treatment with the veterinary medicinal product:

- purulent or haemorrhagic vaginal discharge
- prolonged vaginal discharge lasting over 3 weeks.

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

Nor-steroids are used in humans to induce abortion. Accidental injection may be a particular hazard to women who are pregnant, intending to become pregnant or whose pregnancy status is unknown. Care should be taken by the veterinary surgeon when handling the product and the person restraining the dog to avoid accidental injection. Pregnant women should administer the product with caution. This is an oil-based product that may cause prolonged local reactions at the site of injection. In case of accidental injection, seek urgent medical advice and show the doctor this warning.

Women of child-bearing age should avoid contact with the veterinary medicinal product or wear disposable plastic gloves when administering the veterinary medicinal product.

## 4.6 Adverse reactions (frequency and seriousness)

In bitches treated after 20 days of gestation, abortion is accompanied by the physiological signs of parturition: fetal expulsion, vaginal discharge, reduced appetite, restlessness and mammary congestion. In field trials, 3.4 % of dogs suffered from uterine infections. After induced abortion with the veterinary medicinal product, an early return to oestrus is frequently observed (oestrus - oestrus interval shortened by 1 to 3 months).

Side effects such as anorexia (25 %), excitation (23 %), depression (21 %), vomiting (2 %) and diarrhoea (13 %) have been reported from field trials.

In field trials, the administration of the veterinary medicinal product produced pain during and shortly after injection in 17 % of dogs and a local inflammatory reaction at the injection site in 23 % of dogs. The size and intensity of this reaction depended on the volume of the veterinary medicinal product which was administered. Oedema, skin thickening, local lymph-node enlargement and ulceration may occur. All local reactions are reversible and will usually disappear within 28 days after injection.

In field trials, administration of the veterinary medicinal product induced haematological/biochemical changes in 4.5 % of dogs. These changes were always transient and reversible. The modified haematological parameters were as follows: neutrophilia, neutropaenia, thrombocytosis, haematocrit variation, lymphocytosis, lymphopaenia.

The modified (elevated) biochemical parameters were as follows: urea, creatinine, chloride, potassium, sodium, ALT, ALP, AST.

In rare cases (frequency > 1/10000 and < 1/1000), a hypersensitivity reaction has been/can be observed.

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

Do not administer to pregnant bitches unless it is desirable to terminate the pregnancy.

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

In the absence of available data, a risk of drug interaction between aglepristone and ketoconazole, itraconazole and erythromycin may exist.

As aglepristone is an anti-glucocorticoid, it might reduce the effect of glucocorticoid treatment.

Possible interactions with other medicaments have not been studied.

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

Administer 10 mg per kg of bodyweight of aglepristone, equivalent to 0.33 ml of veterinary medicinal product per kg of bodyweight, twice, 24 hours apart.

Weight of bitch	3 kg	6 kg	9 kg	12 kg	24 kg	30 kg	42 kg
Volume of ALIZIN	1 ml	2 ml	3 ml	4 ml	8 ml	10 ml	14 ml

Inject subcutaneously (only). Severe local reactions can be avoided if the veterinary medicinal product is administered into the scruff of the neck. A light massage of the injection site is recommended.

In large bitches, it is recommended that a maximum of 5 ml is injected at any one site.

This product does not contain an antimicrobial preservative. Swab the septum before removing each dose. Use a dry, sterile needle and syringe.

Following administration of the veterinary medicinal product to dogs, abortion (or resorption) occurs within 7 days.

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

The administration of 30 mg/kg, i.e. 3 times the recommended dose, in bitches showed no adverse effects, except local inflammatory reactions, related to the larger volumes injected.

#### 4.11 Withdrawal Period(s)

Not applicable.

### 5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: antiprogestogen.

ATCvet code: QG03XB90.

## 5.1 Pharmacodynamic properties

Aglepristone is a synthetic steroid counteracting the effect of progesterone by competing with this hormone at the level of the uterine receptors, resulting in abortion (or resorption) within 7 days after administration.

Aglepristone does not modify progesterone, prostaglandins, oxytocin or cortisol plasma concentration within 24 hours after its administration but it induces a discharge of prolactin within 12 hours.

*In vitro*, the affinity of aglepristone for the progesterone receptors in the uterus of the dog is 3 times higher than that of progesterone.

The relative binding affinity of aglepristone to glucocorticoid receptors is similar to that of dexamethasone but aglepristone has antagonistic properties.

## 5.2 Pharmacokinetic properties

After 2 injections of 10 mg/kg/day at a 24-hour interval, the maximal concentration (about 280 ng/ml) is reached after 2.5 days. The mean residence time is around 6 days: this period includes the mean absorption time from the injection site.

After administration of a 10 mg/kg radio-labelled dose, the excretion of radioactivity is very slow. Only 60 % of the administered dose is excreted during the first 10 days and around 80 % over 24 days.

Excretion is essentially *via* the faeces (around 90 %).

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

- Anhydrous ethanol
- Refined arachis oil

### 6.2 Incompatibilities

None known.

Do not mix with other veterinary medical products.

### 6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

Shelf life after first opening the immediate packaging: 28 days.

### 6.4 Special precautions for storage

Keep the vial in the outer carton in order to protect from light.

Should any apparent growth or discoloration occur, the product should be discarded.

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

Vials (glass, type II) of 5 ml, 10 ml or 30 ml for injectable preparations, with bromobutyl stoppers and aluminum caps.

### Presentations:

- box of 1 vial of 5ml, 10ml or 30ml
- box of 10 vials of 10ml.

Not all pack sizes may be marketed.

## **6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials**

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

## **7 MARKETING AUTHORISATION HOLDER**

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1<sup>ère</sup> avenue – 2065 m - L.I.D. –  
06516 Carros Cedex  
France

## **8 MARKETING AUTHORISATION NUMBER(S)**

VPA 10988/066/001

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

26th November 2008

## **10 DATE OF REVISION OF THE TEXT**