

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE****Box containing 1 or 10 vials of lyophilisate and 1 or 10 vials of solvent****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Zoletil 100 (50 mg/ml+50 mg/ml) lyophilisate and solvent for solution for injection

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each ml of reconstituted solution contains:

Tiletamine (as hydrochloride).....50.00 mg

Zolazepam (as hydrochloride).....50.00 mg

**3. PACKAGE SIZE**

1 × 970 mg lyophilisate and 1 × 5 ml solvent

10 × 970 mg lyophilisate and 10 × 5 ml solvent

**4. TARGET SPECIES**

Dogs and cats.

**5. INDICATIONS****6. ROUTES OF ADMINISTRATION**

Intramuscular or intravenous use.

**7. WITHDRAWAL PERIODS****8. EXPIRY DATE**

Exp. {mm/yyyy}

Once reconstituted, use within 7 days.

Once reconstituted, use by: .....

**9. SPECIAL STORAGE PRECAUTIONS**

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

After reconstitution, store in a refrigerator.

<b>10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”</b>
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Read the package leaflet before use.

<b>11. THE WORDS “FOR ANIMAL TREATMENT ONLY”</b>
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For animal treatment only.

<b>12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”</b>
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Keep out of the sight and reach of children.

<b>13. NAME OF THE MARKETING AUTHORISATION HOLDER</b>
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VIRBAC

<b>14. MARKETING AUTHORISATION NUMBERS</b>
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<b>15. BATCH NUMBER</b>
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Lot {number}

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS****Vial of lyophilisate****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Zoletil 100

**2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES**

50 mg/ml + 50 mg/ml

**3. BATCH NUMBER**

Lot {number}

**4. EXPIRY DATE**

Exp. {mm/yyyy}

<b>MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS</b>
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<b>Vial of solvent</b>
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<b>1. NAME OF THE VETERINARY MEDICINAL PRODUCT</b>
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Zoletil 100 solvent



<b>2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES</b>
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5 ml

<b>3. BATCH NUMBER</b>
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Lot {number}

<b>4. EXPIRY DATE</b>
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Exp. {mm/yyyy}

## **B. PACKAGE LEAFLET**

## B. PACKAGE LEAFLET

### 1. Name of the veterinary medicinal product

Zoletil 100 (50 mg/ml + 50 mg/ml) lyophilisate and solvent for solution for injection for dogs and cats

### 2. Composition

Each vial of 970 mg lyophilisate contains:

**Active substances:**

Tiletamine (as hydrochloride) ..... 250.00 mg

Zolazepam (as hydrochloride) ..... 250.00 mg

Each vial of 5 ml solvent contains:

Benzyl alcohol (E1519) ..... 0.100 g

Water for injections ..... up to 5.00 ml

Each ml of reconstituted solution contains:

**Active substances:**

Tiletamine (as hydrochloride) ..... 50.00 mg

Zolazepam (as hydrochloride) ..... 50.00 mg

**Excipient:**

Benzyl alcohol (E1519) ..... 20.00 mg

Appearance of the lyophilisate: White to slightly yellow compact mass.

Appearance of the solvent: Clear colourless liquid.

Appearance of the reconstituted solution: Clear, colourless to slightly green-yellow solution, free from particles.

### 3. Target species

Dogs and cats.

### 4. Indications for use

General anaesthesia.

### 5. Contraindications

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

Do not use in animals with severe cardiac or respiratory disease, or in animals with renal, pancreatic or hepatic insufficiency.

Do not use in the event of severe hypertension.

Do not use in rabbits.

Do not use in animals with head trauma or intracranial tumours.

Do not use for caesarean section.

Do not use in pregnant bitches and queens.

### 6. Special warnings



#### Special warnings:

In dogs, since zolazepam is eliminated more quickly than tiletamine, there is a shorter duration of tranquilisation than there is of anaesthesia.

#### Special precautions for safe use in the target species:

Animals should be fasted for 12 hours prior to anaesthesia.

Remove anti-parasite collar 24 hours before anaesthesia.

If necessary, hypersalivation can be controlled with the administration of anticholinergic agents, such as atropine, before the anaesthesia according to the benefit-risk assessment by the responsible veterinarian.

Please refer to section “Interaction with other medicinal products and other forms of interaction” in case of the use of pre-anaesthetic agents.

Keep anaesthetised animals away from excessive noise and visual stimuli.

Apneustic breathing may be observed more commonly in cats after intravenous injection than after intramuscular injection. Especially for high dosages, such abnormal breathing patterns last for up to 15 minutes and then breathing returns to normal. In case of prolonged apnea respiratory assistance should be provided.

Close observation of dogs during the first 5-10 minutes after induction is recommended especially in animals with cardiopulmonary disease.

The veterinary medicinal product may cause hypothermia, in susceptible animals (small body surface area, low ambient temperature) supplemental heat should be applied if needed.

In dogs and cats the eyes remain open after receiving the product and should be protected from injury and excessive drying of the cornea.

Dosage may need to be reduced in geriatric or debilitated animals, or in animals with renal dysfunction. Reflexes (e.g. palpebral, pedal, laryngeal) are not abolished during anaesthesia and therefore use of this product alone may not be adequate if surgery is performed on these areas.

Redosing may prolong and worsen recovery.

In the event of reinjections, side effects (hyper-reflexia, neurological problems) can be produced due to tiletamine. It is recommended that the recovery phase occur in a calm environment.

The veterinary medicinal product contains benzyl alcohol, which has been documented to cause adverse reactions in neonates. Therefore, the use of the veterinary medicinal product is not recommended in very young animals.

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

In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. Do not drive due to risk of sedation.

Wash splashes from skin and eyes immediately. In case of eye irritation, seek medical advice.

Wash hands after use.

This veterinary medicinal product may cross the placenta and be harmful to the foetus, therefore women who are pregnant, or are suspected to be pregnant, should not use the product.

Benzyl alcohol may cause hypersensitivity (allergic) reactions. People with known hypersensitivity to benzyl alcohol should avoid contact with the product.

#### Pregnancy and lactation:

Laboratory studies in animals have not produced any evidence of teratogenic effects.

The product crosses the placenta and may cause respiratory depression in newborns that can be fatal for puppies and kittens. The safety of the veterinary medicinal product has not yet been established during pregnancy or lactation. Do not use during pregnancy. During lactation, use only according to the benefit-risk assessment by the responsible veterinarian.

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

The benefit-risk assessment for using the product with other pre-anaesthetic or anaesthetic agents must take into consideration the dosages of the agents used, the nature of the intervention and the ASA (American Society of Anaesthesiologists) class to which the animal belongs. The required dosage of tiletamine-zolazepam is likely to change depending on which agents are concurrently used.

The dosage of tiletamine – zolazepam may need to be reduced when used concomitantly with pre-anaesthetic and other anaesthetic agents. Premedication with phenothiazine tranquilisers (e.g. acepromazine) can cause increased cardio-respiratory depression and an increased hypothermic effect that occurs in the last phase of anaesthesia.

Do not use medications containing chloramphenicol during the pre- or intra-operative period, as this slows down elimination of the anaesthetics.

#### Overdose:

100 mg per kg constitutes a lethal dose for cats and dogs when administered intramuscularly, i.e., 5 to 10 times the anaesthetic dose. In the event of an overdose, and in obese or old animals, recovery may be slower.

Overdosed animals must be monitored carefully. The signs of overdosage are mainly cardio-respiratory depression that can appear from 20 mg/kg depending on the animal's health, the level of central nervous system depression, and whether hypothermia is present. An earlier warning sign of overdosage is the loss of cranial and spinal reflexes. Prolongation of the anaesthesia can be produced. There is no specific antidote and treatment is symptomatic. Doxapram may have antagonistic activity against the tiletamine-zolazepam, increasing both heart and respiratory rates and reducing the arousal time.

#### Major Incompatibilities:

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

## **7. Adverse events**

Dogs and cats:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Immediate pain upon injection <sup>1</sup> Neurological disorder (Convulsions, Coma, Hyperaesthesia) <sup>2</sup> , Prolonged anaesthesia (Myoclonus, Ataxia, Paresis, Restlessness) <sup>3</sup> Respiratory tract disorder (Dyspnoea, Tachypnoea, Bradypnoea) <sup>2, 4</sup> Cardiac disorder (Tachycardia) <sup>2, 4</sup> Systemic disorder (Prostration, Hypothermia, Hyperthermia) <sup>2</sup> , Cyanosis <sup>2, 4</sup> Pupil disorder <sup>2</sup> Hypersalivation <sup>2</sup> Agitation <sup>2</sup> , Vocalisation <sup>2</sup>

<sup>1</sup> Most prevalent in cats.

<sup>2</sup> Mainly during the awakening phase in the dog, and during surgery and the awakening phase in the cat.

<sup>3</sup> Observed during the recovery phase.

<sup>4</sup> At doses of 20 mg/kg and above.

These adverse effects are reversible and disappear once the active substance is eliminated from the body.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

## **8. Dosage for each species, routes and method of administration**

Intramuscular or intravenous use.

Dosage:

The content of the lyophilisate vial is to be diluted in 5 ml of the attached solvent.

The dosage is expressed in mg of the product, on the understanding that the reconstituted product is at a concentration of 100 mg per ml and contains 50 mg of tiletamine per ml and 50 mg of Zolazepam per ml.

When the product is administered intramuscularly (unable to stand in 3 to 6 minutes) or intravenously (unable to stand in less than one minute), the recommended therapeutic dosages are the following:

<b>IN DOGS</b>	<b>Intramuscular route</b>	<b>Intravenous route</b>
Tests and procedures causing little pain	7 to 10 mg/kg bw 0.07 to 0.1 mL/kg bw	5 mg/kg bw 0.05 mL/kg bw
Minor surgical procedures, anaesthesia of short duration	10 to 15 mg/kg bw 0.1 to 0.15 mL/kg bw	7.5 mg/kg bw 0.075 mL/kg bw
Painful interventions	15 to 25 mg/kg bw 0.15 to 0.25 mL/kg bw	10 mg/kg bw 0.1 mL/kg bw

<b>IN CATS</b>	<b>Intramuscular route</b>	<b>Intravenous route</b>
Tests and procedures causing little pain	10 mg/kg bw 0.1 mL/kg bw	5 mg/kg bw 0.05 mL/kg bw
Orthopaedic operation	15 mg/kg bw 0.15 mL/kg bw	7.5 mg/kg bw 0.075 mL/kg bw

Please refer also to sections “Adverse events” and/or “Overdose” since adverse reaction might occur at therapeutic doses.

Intravenous injections to be repeated, if needed, at between 1/3 and 1/2 of the initial dose but the total dosage should not exceed 26.4 mg/kg bw (0.264 mL/kg bw)..

The individual response to Tiletamine-Zolazepam will vary depending upon several factors.

Therefore, the dosage should be adjusted, at the discretion of the practitioner, based on the species, the type and duration of surgical procedure, the other concomitant medication (pre-anaesthetic and other anaesthetic agents) and the health status of the animal (age, obesity, severe organic deficiencies, state of shock, debilitating diseases).

Duration of anaesthesia: 20 to 60 minutes depending on dose.

The product should not be used as sole anaesthetic agent for painful operations. For these operations the product should be combined with an appropriate analgesic.

## **9. Advice on correct administration**

### Pre-surgical preparation:

As for all anaesthetics animals should be fasted for at least 12 hours before anaesthesia.

In dogs and cats, the use of atropine, subcutaneously, 15 minutes before injection, may be considered.

### Recovery period:

Analgesia lasts longer than surgical anaesthesia. Return to normal is progressive and can last 2 to 6 hours in a calm environment (avoid excessive noise and light). Recovery may be delayed due to an overdose in obese, old or debilitated animals.

## **10. Withdrawal periods**

Not applicable.

## **11. Special storage precautions**

Keep out of the sight and reach of children.

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

After reconstitution, store in refrigerator (2°C - 8°C).

Do not use this veterinary medicinal product after the expiry date which is stated on the carton and vial label after Exp. The expiry date refers to the last day of that month.

Shelf life after reconstitution according to directions: 7 days between 2°C and 8°C.

## **12. Special precautions for disposal**

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

## **13. Classification of veterinary medicinal products**

Veterinary medicinal product subject to prescription.

## **14. Marketing authorisation numbers and pack sizes**

1 vial of 970 mg lyophilisate and 1 vial of 5 ml solvent.

10 vials of 970 mg lyophilisate and 10 vials of 5 ml solvent.

Not all pack sizes may be marketed.

## **15. Date on which the package leaflet was last revised**

Detailed information on this veterinary medicinal product is available in the [Union Product Database \(https://medicines.health.europa.eu/veterinary\)](https://medicines.health.europa.eu/veterinary).

**16. Contact details**

Marketing authorisation holder and manufacturer responsible for batch release and contact details to report suspected adverse reactions:

VIRBAC  
1<sup>ère</sup> avenue 2065 m LID  
06516 Carros  
France

Local representatives and contact details to report suspected adverse reactions:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

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