Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Dopram-V 20 mg/ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active Substance

Doxapram Hydrochloride	20 mg
(equivalent to 17.5mg/ml doxapram)	

Excipients

Chlorobutanol hemihydrate (preservative)	5 mg

For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection or sublingual use.

A clear colourless solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Dogs, cats, horses, calves and lambs.

4.2 Indications for use, specifying the target species

Respiratory stimulant

For dogs, cats and horses:

1. To stimulate respiration during and after general anaesthesia.
2. To speed awakening and return of reflexes after anaesthesia, when this is considered beneficial.

Neonate dogs, cats, calves and lambs:

1. To initiate respiration following dystocia or Caesarean section.
2. To stimulate respiration following dystocia or Caesarean section.

4.3 Contraindications

Do not use in food producing animals with the exception of neonatal calves, lambs and horses.

4.4 Special warnings for each target species

No special warnings apart from use in dogs which have been sedated with morphine (see 4.5).

4.5 Special precautions for use

Special precautions for use in animals

Dosage of Dopram-V should be adjusted to meet the requirements of the situation. Adequate, but not excessive, doses should be used. A patent airway is essential. Reflexes should be checked periodically.

Excessive doses may produce hyperventilation which may be followed by reduced carbon dioxide tension in the blood, cerebral vasoconstriction, hypoxia, and possible brain damage.

Excessive doses administered to animals, during or following anaesthesia with cyclopropane or halogenated hydrocarbon anaesthetics, may precipitate cardiac arrhythmias.

Dopram-V should be used with extreme caution in dogs which have been sedated with morphine. Administration of Dopram-V at a dose of 10mg/kg to such animals may be followed by convulsions.

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

Avoid self-injection with the product.
Avoid direct contact with skin and eyes.
Do not smoke, eat or drink when using the product.
Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

No significant side effects at recommended dosage.

4.7 Use during pregnancy, lactation or lay

Foetal toxicity studies with doxapram in the rat and rabbit have not revealed any teratogenic effects, nor evidence of any effect on male or female fertility. Not intended for use in animals producing milk for human consumption.

4.8 Interaction with other medicinal products and other forms of interaction

(See also section 4.5 above)

The respiratory stimulant effects of doxapram in the dog were not blocked by anaesthetic doses of phenobarbitone sodium, pentobarbitone sodium, thiobarbitone sodium or secobarbitone sodium.

The respiratory depressant effects of morphine and pethidine were antagonised by doxapram in the cat and dog. In the cat, convulsions occurred after administration of morphine and doxapram but this species is highly susceptible to the convulsant activity of morphine.

Doxapram antagonised the spinal neuronal depressant effects of chlorpromazine, mephenesin and methocarbamol in non-anaesthetised cats.

Reversal of the respiratory depressant effects of large doses of ethanol was produced after administration of doxapram to rabbits and dogs.

Blood ethanol concentration was studied in the rat 2 - 3 hours after the concomitant administration of ethanol and doxapram. The blood ethanol concentration in the doxapram-treated animals was found to be significantly lower than that of the control animals.

The respiratory stimulant and pressor effects of doxapram were markedly potentiated by prior treatment with nialamide. Potentiation after pre-treatment with other monoamine oxidase inhibitors has not been studied.

4.9 Amounts to be administered and administration route

To ensure adequate dosing an insulin-type syringe must be used for administration to low bodyweight animals.

Post anaesthetic use: For intravenous use only.

Dogs and cats:
Following intravenous anaesthesia 2-5 mg/kg (0.1 - 0.25ml/kg) depending on response. Following inhalation anaesthesia 1-2mg/kg (0.05 - 0.1ml/kg) depending on response. Dosage should be adjusted for depth of anaesthesia and degree of respiratory depression. Dosage can be repeated in 15 to 20 minutes if necessary.

Horses:
Following intravenous or inhalation anaesthesia 0.5-1.0mg/kg (2.5-5.0ml/100kg) depending on response.
Dosage should be adjusted for depth of anaesthesia and degree of respiratory depression.

Neonatal use:

Puppies:
For intravenous or subcutaneous injection and for topical sublingual use.
1-5mg (0.05-0.25ml) depending on size of neonate and degree of respiratory depression.

Kittens:
For intravenous or subcutaneous injection and for topical sublingual use.
1-2mg (0.05-0.1ml) depending on size of neonate and degree of respiratory depression.

Calves:
For intravenous, intramuscular, subcutaneous or sublingual use. 40-100mg (2.0-5.0ml) depending on size of neonate and degree of respiratory depression.

Lambs:
For intravenous, subcutaneous or sublingual use.
5-10mg (0.25-0.5ml) depending on size of neonate and degree of respiratory depression.

The action of Dopram-V is rapid, usually beginning in a few seconds. The duration and intensity of response depends upon the dose, the condition of the animal at the time the drug is administered, and depth of anaesthesia. Repeated doses should not be given until the effects of the first dose have passed, and the condition of the patient requires it.

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

See 4.5 above (special precautions for use).
In trials carried out on conscious cats to determine the total dose required to initiate hyperventilation compared to the total dose required to produce convulsions, the convulsive dose to respirogenic dose was calculated to be 38 : 1.

4.11 Withdrawal Period(s)

Horses and neonatal calves and lambs:
Meat and offal: 28 days.
Not intended for use in animals producing milk for human consumption.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Respiratory stimulants

ATC vet code: QR07AB01

5.1 Pharmacodynamic properties

Published papers and a 1963 A.H. Robins report (Alphin et al) refer to the effect of doxapram on the respiratory system.

Doxapram administered to dogs was found to increase minute volume primarily by an increase in tidal volume with a concomitant increase in PaO_2, a decrease in $PaCO_2$ and an increase in arterial pH.

The same 1963 A.H. Robins report (Alphin et al) and further published papers cover the site and mechanism of action of doxapram. The evidence suggests that the action of doxapram is two-fold depending on the dose administered. Firstly, chemoreceptor stimulation results in a specific increase in the activity of the respiratory neurones in the medulla. Secondly, as the dose is increased, then non-specific central stimulation is superimposed upon these actions.

In addition, further references give information on the effect of doxapram on the cardiovascular system, cerebral blood flow, the pituitary-adrenal axis, renal blood flow, gastric secretion and various enzyme systems. The effect of doxapram in haemorrhagic shock is also referred to, as is the convulsant activity of doxapram.

5.2 Pharmacokinetic properties

The metabolism of doxapram has been studied in the rat, dog and man. Doxapram is extensively metabolised; the metabolites and unchanged doxapram are excreted in the bile and urine. The pharmacokinetic properties of doxapram can be described by a multi-compartmental model. Due to rapid redistribution the pharmacological effects of an intravenous injection of doxapram are terminated within 15-20 minutes following administration.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Chlorobutanol Hemihydrate
Water for Injections

6.2 Incompatibilities

The product is incompatible with alkaline solutions such as aminophylline, frusemide and thiopentone.

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 2years.

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

6.4 Special precautions for storage

Do not store above 25°C.
Do not freeze.
Protect from light.
Keep the container in the outer carton.

6.5 Nature and composition of immediate packaging

20ml multidose glass vial with butyl rubber bung and aluminium overseal.

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

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

7 MARKETING AUTHORISATION HOLDER

Zoetis Ireland Limited
25/28 North Wall Quay
Dublin 1
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10438/025/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st October 2000

Date of last renewal: 30th September 2010

10 DATE OF REVISION OF THE TEXT

July 2011
January 2013