SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Fentadon 50 microgram/ml solution for injection for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each1 ml solution contains:

Active substance:
Fentanyl 50 microgram
(equivalent to fentanyl citrate 78.5 microgram)

Excipients:

Methyl parahydroxybenzoate (E218)	1.6 mg
Propyl parahydroxybenzoate	0.2 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Target species

Dogs.

4.2 Indications for use, specifying the target species

For intra-operative analgesia during surgical procedures such as soft tissue and orthopaedic surgery.
For the control of post-operative pain associated with major orthopaedic and soft tissue surgery.

4.3 Contraindications

Do not use in case of hypersensitivity to the active substance, or to any of the excipients.
Do not use in dogs with cardiac failure, hypotension, hypovolaemia, obstructive airway disease, respiratory depression, hypertension or with a history of epilepsy.
Do not use in animals with severe liver or renal dysfunction.
Refer to sections 4.7 and 4.8.

4.4 Special warnings for each target species

The use of this veterinary medicinal product must be preceded by a thorough clinical examination. Atropine may be used to block the vagal effects.

4.5 Special precautions for use

Special precautions for use in animals

This veterinary medicinal product should be titrated for the individual animal to an effective dose that provides adequate analgesia and minimises undesirable effects. Animals should be carefully monitored until an effective dose is reached. Due to individual differences in pain sensitivity, the effects of fentanyl may be variable. Older animals may tend to titrate to a lower effective dose than younger animals.
It is important when estimating the required dose for intra-operative analgesia to assess the likely degree of surgical stimulation, the effect of premedication drugs, whether supportive care like endotracheal intubation and ventilatory support may be required, and the duration of the procedure.
If other narcotic or CNS-depressant drugs (e.g. propofol, isoflurane, sevoflurane) are used concurrently with fentanyl the doses of these agents may need to be reduced.
When estimating the required dose for post-operative analgesia the degree of tissue damage has to be assessed.
As a class, opioids, including this veterinary medicinal product, may cause hypothermia with duration related to dose, bradypnea, hypotension and bradycardia. Therefore, animals should be continuously monitored for rectal temperature, pulse rate, respiratory rate and heart rhythm during surgical anaesthesia.
In case of renal, cardiac or hepatic dysfunction, hypovolaemia or shock, there may be greater risk associated with the use of the product. It is desirable to reduce dosage in case of hypothyroidism and in case of chronic hepatic or renal disease. As with all narcotic analgesics, care should be taken when administering fentanyl to animals with myasthenia gravis.
Facilities for the maintenance of a patent airway, intermittent positive pressure ventilation (IPPV) and oxygen supplementation should be available. When respiratory depression occurs, controlled ventilation should be installed.
As with all potent opioids, profound analgesia is accompanied by respiratory depression, which may persist into or recur in the early post-operative period. The respiratory depressant effects may be more problematic in animals with pre-existing respiratory disease or increased intracranial pressure. The effect of an opioid on head injury is dependent on the type and severity of the injury and the respiratory support supplied. It is imperative to ensure that adequate spontaneous breathing has been established and maintained before discharge from the recovery area whenever large doses of infusions of fentanyl have been administered. The benefit/risk ratio for using the product should be made by the attending vet. The pharmacological effects of fentanyl citrate can be reversed by naloxone.

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

-Fentanyl, an opioid, may cause adverse effects after internal exposure, including respiratory depression or apnoea, sedation, hypotension and coma.
The product may cause hypersensitivity reactions. Avoid contact with the skin and eyes. Wear protective gloves when handling the product. Wash hands after use.

Wash any splashes from skin and eyes immediately with large amounts of water. Remove contaminated clothes.
Care should be taken to avoid accidental self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet to the doctor but DO NOT DRIVE as sedation may occur.
-Adverse effects on the foetus cannot be excluded. Pregnant women should avoid handling the product. In case of women who are breastfeeding being accidentally exposed, breastfeeding is discouraged for 24 hours, as fentanyl may transfer to breast milk.

ADVICE TO DOCTORS:
Fentanyl is an opioid whose toxicity may cause clinical effects, including respiratory depression or apnoea, sedation, hypotension and coma. When respiratory depression occurs, controlled ventilation should be installed. Administration of the opioid antagonist naloxone to reverse the symptoms is recommended.

4.6 Adverse reactions (frequency and seriousness)

In analogy with other narcotic analgesics, common serious adverse reactions with fentanyl are respiratory depression and bradycardia. Bradycardia may occur due to increased cardiac vagal stimulation. The respiratory depressant effects can be of long duration and may exhibit a biphasic pattern.

Also common is a transient fall in blood pressure following intravenous administration of fentanyl citrate injection even at doses of 2.5 - 5 µg/kg. Hypothermia may occur. Lowered nociceptive thresholds in dogs when the effects of the drug dissipate have been described.

The following adverse reactions have been observed during studies with the product and occur very commonly:
Rapid breathing, panting, urination, defecation, vocalization, tongue protrusion, over-activity, irritability, body tremors, vomiting, scratching and sedation.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10.000 animals, including isolated reports)

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation. The use of the product is not recommended during pregnancy or lactation.
Laboratory studies in rats have not produced any evidence of a teratogenic, foetotoxic or mutagenic effect. Placental transfer of fentanyl occurs. Administration during parturition may cause respiratory depression in the foetus.

4.8 Interaction with other medicinal products and other forms of interaction

Fentanyl is a potent anaesthetic sparing substance. To avoid anaesthetic overdose in dogs treated with the veterinary medicinal product, anaesthetic agents should be administered only until the desired effect is produced.
The veterinary medicinal product should be used with caution in conjunction with morphine or other opioid type analgesics as the effects have not been studied.
The effects of the concomitant use of the veterinary medicinal product and α-adrenergic agonists have not been studied. Therefore, α2-adrenergic agonists should be used with caution in animals dosed with the veterinary medicinal product due to potentially additive or synergistic effects.

4.9 Amounts to be administered and administration route

For intravenous administration. The weight of the animal to be treated should be accurately determined before the administration of the product. Onset of action is seen within 5 minutes. The duration of the analgesic effect is 20 (lowest recommended dose) to 40 minutes (highest recommended dose).

Fentanyl can be administered according to the following dosage regimen:

Analgesia by Continuous Rate Infusion (CRI)

- 5 - 10 µg/kg (0.1 - 0.2 ml/kg) IV as a bolus, followed by 12 - 24 µg/kg/hr (0.24 - 0.48 ml/kg/hr) IV for intra-operative analgesia as CRI.
- 6 - 10 µg/kg/hr (0.12 - 0.2 ml/kg/hr) IV for subsequent post-operative analgesia as CRI in sedated animals. During post-operative CRI administration of fentanyl, animals should be monitored carefully.

Chemical-physical compatibility has only been demonstrated for dilutions 1:5 with the following solutions for infusion: sodium chloride 0.9%, Ringer's solution and glucose 5%.

The veterinary medicinal product has a narrow margin of safety and it is important to measure the dose accurately to avoid overdosing.

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

A 2 fold overdose as a bolus injection resulted in the effects mentioned in section 4.6. In the event that any of the following observations are made following the application/overdose of the product, reversal should be initiated: severe sedation, unconsciousness, seizures, laboured or abdominal breathing or severe hypotension. The specific narcotic antagonist naloxone hydrochloride can be used to counteract respiratory depression. A dose of 0.01 to 0.04 mg/kg is given intravenously and may be repeated at intervals of 2 to 3 minutes if necessary.

4.11 Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Analgesics. Opioids. Phenylpiperidine derivatives.
ATCvet code: QN02AB03.

5.1 Pharmacodynamic properties

Fentanyl is a synthetic opioid that is selective for the μ-opioid receptor.
Fentanyl citrate has the ability to produce profound analgesia. It causes only minor heart and circulatory depression.
The principal actions of therapeutic value are analgesia and sedation.
Following intravenous injection fentanyl has a rapid onset of action, although the maximal analgesic and respiratory depressant effects may not occur for several minutes.

5.2 Pharmacokinetic particulars

After intravenous injection the fentanyl plasma concentrations decrease rapidly primarily due to redistribution. In dogs, fentanyl is 60% bound to plasma proteins. Fentanyl has a large volume of distribution of more than 5 l/kg. The plasma kinetics of fentanyl are independent of the dose in the range of recommended doses. Fentanyl has a relatively long elimination half-life: 45 minutes to more than 3 hours in dogs. The clearance is high about 40 to 80 ml/min/kg. It is primarily eliminated by metabolism, with hydroxylation and dealkylation being the primary mechanisms, and less than 8% of the total dose is eliminated as unchanged drug. In addition to hepatic metabolism fentanyl may be metabolised in extra hepatic sites and eliminated by extra renal routes.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate
Sodium chloride
Hydrochloric acid (for pH-adjustment)
Sodium hydroxide (for pH-adjustment)
Water for injections

6.2 Incompatibilities

Do not mix with any other veterinary medicinal product except the infusion solutions indicated in section 4.9.
The product is incompatible with injection fluids containing meloxicam or any other non-aqueous solution.

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.

Chemical and physical stability of the dilutions (as indicated in section 4.9) has been demonstrated for 4 hours at 25°C. From a microbiological point of view the dilutions should be used immediately.

6.4 Special precautions for storage

Do not freeze.

6.5 Nature and composition of immediate packaging

Vials of uncoloured glass type I, filled with 5, 10, 20, 25, 30, 50 and 100 ml. Teflon-coated chlorobutyl rubber stoppers type I secured with aluminium caps.

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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Eurovet Animal Health B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands

8. MARKETING AUTHORISATION NUMBER

Vm 16849/4031

9. DATE OF FIRST AUTHORISATION

27 February 2012

10. DATE OF REVISION OF THE TEXT

March 2017

PROHIBITION OF SALE, SUPPLY AND/OR USE

This product falls within the regime of controlled drugs Schedule II

Approved: 24 March 2017