Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Buprelieve Multidose 0.3 mg/ml Solution for Injection for Dogs, Cats and Horses

Date Created: September 2016

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Buprelieve Multidose 0.3 mg/ml Solution for Injection for Dogs, Cats and Horses
Applicant	Jurox (UK) Limited Second Floor, Richmond House 105 High Street Crawley West Sussex RH10 1DD United Kingdom
Active substance	Buprenorphine 0.3 mg, as buprenorphine hydrochloride 0.324 mg
ATC Vetcode	QN02AE01
Target species	Dogs, cats, horses
Indication for use	Post-operative analgesia in the dog, cat and horse. Potentiation of the sedative effects of centrally-acting agents in the dog and horse. When used in horses, an intravenous sedative should be administered within five minutes prior to injection of buprenorphine.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 13 (1) of Directive 2001/82/EC as amended.

I. SCIENTIFIC OVERVIEW

This was an application for a generic product, submitted in accordance with Article 13 (1) of Directive 2001/82/EC, as amended. The reference product is Vetergesic Multidose 0.3 mg/ml Solution for Injection for Dogs, Cats and Horses, marketed in the UK since February 2009. By way of a biowaiver, the applicant did not need to submit bioequivalence studies as the proposed product was deemed to be essentially similar to the reference product under 7.1a) and 7.1b) of the CVMP guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/00-Rev.2).

The product is indicated for use as a post-operative analgesic in in dogs, cats and horses. In dogs, the product is administered by intramuscular or intravenous injection. For the potentiation of sedation and post-operative analgesia, the dose is 10 – 20 µg/kg, (0.3 – 0.6 ml/ 10kg). If necessary, for further pain relief, repeat after 3 - 4 hours with 10 µg/kg or after 5 – 6 hours with 20 µg/kg.

For cats, the product is administered also by intravenous or intramuscular injection. The product is not used for the potentiation of sedation in cats. For post-operative analgesia, the dose is 10 – 20 µg/kg, (0.3 – 0.6 ml/10 kg). If necessary, repeat after 1 - 2 hours.

For horses, the product is administered by intravenous injection only. For the potentiation of sedation, the dose is 5 µg/kg, (1.7 ml/ 100 kg), minutes after administration of an intravenous sedative. The dose may be repeated after 10 minutes. For post-operative analgesia, the dose is 10 µg/kg (3.3 ml/100 kg), 5 minutes after administration of an intravenous sedative. If necessary, the dose for post-operative analgesia may be repeated once, after not less than 1 – 2 hours.

The product is produced and controlled using validated methods and tests which ensure the consistency of the product released on the market. It has been shown that the product can be safely used in the target species, any reactions observed are indicated in the SPC.[1] The product is safe for the user and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy [2] of the product was demonstrated

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains buprenorphine 0.3 mg as buprenorphine hydrochloride 0.324 mg, and the excipients benzethonium chloride*, glucose anhydrous, hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment) and water for injections.

The container/closure system consists of 10 ml amber Type I glass vials with a rubber stopper. The vial is fitted with an aluminium collar with a plastic flip-off cap. The particulars of the containers and controls performed are provided and conform to the regulation. The choice of the formulation and the presence of preservative are justified.

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

II.B. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing method consists of the heating of water with the addition of chlorocresol, the addition of glucose anyhydrous. This is followed by addition of the active substance, with adjustment of pH and filling to volume. The product is then transferred to the sterilised vials.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

II.C. Control of Starting Materials

The active substance is buprenorphine, as buprenorphine hydrochloride, an established active substance described in the European Pharmacopoeia (Ph. Eur). The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided. An appropriate certificate of suitability was provided.

All excipients are monographed in the Ph. Eur, and have historically been used in veterinary medicinal products. Suitable specifications for the excipients were provided.

*Change of excipient from chlorocresol to benzethonium chloride via variation procedure February 2020.

All packaging was suitably assessed. The vials confirm to a monograph within the Ph. Eur.

II.C.4. Substances of Biological Origin

A transmissible spongiform encephalopathy (TSE) declaration confirming that the product complies with the 'Note for Guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products' (EMEA/410/01 rev 3).

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.E. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product. Satisfactory validation data for the analytical methods have been provided. Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification. Control tests on the finished product include those for appearance, clarity, identification and assay of the active substance and chlorocresol, the detection of impurities, pH value and sterility of the product.

II.F. Stability

Stability data on the active substance and finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions. A re-test period of 3 years was agreed. Suitable stability studies on the active substance were presented, with product stored in accordance with VICH conditions for a variety of time periods up to 36 months. Product was stored for various time periods at 25^{o}C/60% RH, 30^{o}C/65% RH and 40^{o}C/75% RH.

G. Other Information

Shelf-life of the veterinary medicinal product as packaged for sale: 30 months
Shelf-life after first opening the immediate packaging: 28 days
Do not store above 25ºC.
Keep the vial in the outer carton in order to protect from light.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13 (1), and the product is accepted as being essentially similar under a biowaiver to the reference product, results of pharmacological and toxicological tests are not required.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users, the environment and consumers.

III.A Safety Documentation

User Safety

A user risk assessment was provided in compliance with the relevant guideline. Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. The warnings are identical to those of the reference product:

- Wash hands/affected area thoroughly after any accidental spillage.
- As buprenorphine has opioid-like activity, care should be taken to avoid self-injection. In case of accidental self-injection or ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
- Following eye contamination or skin contact, wash thoroughly with cold running water. Seek medical advice if irritation persists.

Environmental Safety

A Phase I environmental risk assessment was provided. The product will only be used predominantly in non-food animals, in individual animals and as such the risk environmental exposure will be low. A Phase II ERA was not required. As the active substance is a controlled drug, the disposal advice on the SPC and product literature was updated to include:

- Any unused product must be disposed of in accordance with the Misuse of Drugs Regulations (2001).

III.B.2 Residues documentation

Residue Studies

No residue depletion studies were conducted because the product is for use in non-food producing animals only. The SPC and product literature carry the warning:

- Not authorised for use in horses intended for human consumption.

IV CLINICAL DOCUMENTATION

As this is a generic application according to Article 13 (1), and the product is accepted as being essentially similar to the reference product under a biowaiver, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product. No further assessment was required.

V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the benefit/risk profile of the product(s) is favourable.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)