



**Veterinary  
Medicines  
Directorate**

**United Kingdom  
Veterinary Medicines Directorate  
Woodham Lane  
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Surrey KT15 3LS**

**NATIONAL PROCEDURE**

**PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY  
MEDICINAL PRODUCT**

**ButorVet 10 mg/ml Solution for Injection for Horses, Dogs and Cats**

**Date Created: March 2025**

## MODULE 1

### PRODUCT SUMMARY

Name, strength and pharmaceutical form	ButorVet 10 mg/ml Solution for Injection for Horses, Dogs and Cats, Solution for injection
Applicant	C&H Generics Ltd, c/o Michael McEvoy and Co, Seville House, New Dock Street, Galway, Ireland
Active substance	Butorphanol
ATC Vet code	QN02AF01
Target species	Cats Dogs Horses
Indication for use	<p><b>Horse</b></p> <p>As an analgesic:</p> <ul style="list-style-type: none"><li>• For the relief of moderate to severe abdominal pain associated with colic of gastrointestinal origin.</li></ul> <p>As a sedative:</p> <ul style="list-style-type: none"><li>• For sedation, given after the administration of certain alpha2-adrenoceptor agonists (detomidine, romifidine)</li></ul> <p><b>Dog</b></p> <p>As an analgesic:</p> <ul style="list-style-type: none"><li>• For the relief of moderate visceral pain in dogs.</li></ul> <p>As a sedative:</p> <ul style="list-style-type: none"><li>• For sedation in conjunction with certain alpha2-adrenoceptor agonists (medetomidine)</li></ul>

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	<p>As a premedicant prior to general anaesthesia:</p> <ul style="list-style-type: none"><li>• For use as a premedicant as a sole agent or in combination with acepromazine. A dose-related reduction in the dose of induction-anaesthetic agent (propofol) is also provided.</li></ul> <p>As an anaesthetic:</p> <ul style="list-style-type: none"><li>• For anaesthesia when used in combination with medetomidine and ketamine.</li></ul> <p><b>Cat</b></p> <p>As an analgesic for the relief of moderate pain:</p> <ul style="list-style-type: none"><li>• For pre-operative use to provide analgesia during surgery.</li><li>• For post-operative analgesia after small surgical procedures.</li></ul> <p>As a sedative:</p> <ul style="list-style-type: none"><li>• For sedation when used in combination with certain alpha2-adrenoceptor agonists (medetomidine).</li></ul> <p>As an anaesthetic:</p> <ul style="list-style-type: none"><li>• For anaesthesia, when used in combination with medetomidine and ketamine, suitable for short painful anaesthetic procedures.</li></ul>
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## **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](http://www.gov.uk/check-animal-medicine-licensed)

## MODULE 3

### PUBLIC ASSESSMENT REPORT

Legal basis of original application	Generic application in accordance with Article 8 of VMRs 2013 (Schedule 1, Para 10) as amended.
Date of conclusion of the procedure	18/03/2025

#### I. SCIENTIFIC OVERVIEW

This is a generic application in accordance with Article 8 of VMRs 2013 (Schedule 1, Para 10) as amended, for authorisations in Great Britain (GB) and Northern Ireland (NI). The reference product in GB is Torbugesic 10 mg/ml Solution for Injection, authorised via a national procedure in May 1991. The reference product in NI is Torbugesic 10 mg/ml Solution for Injection, authorised in the EU in October 2000. These reference products were accepted as essentially similar to the application product in accordance with section 7.1.d) of the Guideline on the conduct of bioequivalence studies for veterinary medicinal products (EMA/CVMP/016/2000-Rev.4).

ButorVet 10 mg/ml solution for injection for horses, dogs and cats contains 10 mg of butorphanol (as butorphanol tartrate) per ml of product.

This product is indicated for use in cats and dogs as an analgesic, sedative and anaesthetic. In dogs it may also be used for pre-medication prior to general anaesthesia. In horses, this product is indicated as an analgesic and sedative. For cats and dogs, the product can be administered via intravenous, intramuscular and subcutaneous use. In horses the product is administered by intravenous injection only. For amounts to be administered please refer to Section 3.9 of the SPC<sup>1</sup>.

The distribution category in GB and NI is POM-V, a veterinary medicinal product subject to prescription.

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<sup>1</sup>. The product is safe for the user, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy<sup>2</sup> of the product was demonstrated according to the claims made in

<sup>1</sup> SPC – Summary of product Characteristics.

<sup>2</sup> Efficacy – The production of a desired or intended result.

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 butorphanol (as butorphanol tartrate) and the excipients benzethonium chloride, citric acid monohydrate, sodium citrate, sodium chloride and water for injections

The container/closure system consists of a Type I clear glass multi-dose vial, with chlorobutyl rubber stoppers secured with an aluminium 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 regulatory 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 manufacture of the bulk, filtration, primary packaging and terminal sterilisation.

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

### ***II.C. Control of Starting Materials***

The active substance is butorphanol, an established active substance described in the United States Pharmacopeia (USP) and supported by an ASMF (Active Substance Master File). 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.

The excipients of the formulation are well known pharmaceutical ingredients covered by Ph. Eur. monographs. All the components are routinely used in the manufacture of this pharmaceutical form. Microbial control is included for majority of the excipients and the testing of excipients is considered appropriate.

The container/closure system is a clear glass multi-dose vial, with chlorobutyl rubber stoppers secured with an aluminium cap, which is adequate for the intended use of the medicinal product.

#### ***II.C.4. Substances of Biological Origin***

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this product.

#### ***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 are those appropriate for this pharmacological form.

#### ***II.F. Stability***

Stability data on the active substance have been provided in accordance with applicable regulatory guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

Stability data on the finished product have been provided in accordance with applicable regulatory guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

#### ***G. Other Information***

The shelf life of the veterinary medicinal product as packaged for sale is 4 years. The shelf life after first opening the immediate packaging is 30 days. The product should be stored below 25°C.

### **III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACOTOXICOLOGICAL)**

As this is a generic application and bioequivalence with the reference products were accepted due to essential similarity, no new pharmacological and toxicological tests are required.

Warnings and precautions as listed on the product literature are in line with the reference products, with the addition of a user warning regarding the effects of

accidental self-injection. This was added as the warning has been included in recently authorised products of the same pharmaceutical form, with the same concentrations of the active substance.

The warnings and precautions are adequate to ensure safety of the product to users/consumers/the environment.

### **III.A Safety Documentation**

#### **Pharmacological Studies**

Bioequivalence with the reference products were accepted due to essential similarity.

Butorphanol tartrate is a centrally acting analgesic. Its action is agonist-antagonist at the opiate receptors in the central nervous system; agonist at the kappa ( $\kappa$ ) opioid receptor subtype and antagonist at the mu ( $\mu$ ) receptor subtype. The kappa ( $\kappa$ ) receptors control analgesia, sedation without depression of cardiopulmonary system and body temperature, whereas the mu ( $\mu$ ) receptors control supraspinal analgesia, sedation and depression of cardiopulmonary system and body temperature. The agonist component of butorphanol activity is ten times more potent than the antagonist component.

Analgesia generally occurs within 15 minutes following administration in horses, dogs and cats. After a single intravenous dose in the horse, analgesia usually lasts for 15 –60 minutes. In the dog, it lasts for 15 - 30 minutes after a single intravenous administration. In cats with visceral pain, analgesic effect for 15 minutes up to 6 hours after butorphanol administration has been demonstrated. In cats with somatic pain, the duration of analgesia has been considerably shorter.

In the horse, butorphanol has a high clearance (on average 1.3 L/h.kg) after intravenous administration. It has a short terminal half-life (mean <1 hour), indicating that 97% of a dose will be eliminated after intravenous administration in, on average, less than 5 hours.

In the dog, butorphanol administered by the intramuscular route has a high clearance (around 3.5 L/h.kg). It has a short terminal half-life (mean <2 hours), indicating that 97% of a dose will be eliminated after intramuscular administration in, on average, less than 10 hours. Repeated dose pharmacokinetics and the pharmacokinetics following intravenous administration have not been studied.

In the cat, butorphanol administered by the subcutaneous route has a low clearance (<1.32 L/h.kg). It has a relatively long terminal half-life (around 6 hours) indicating that 97% of the dose will be eliminated in approximately 30 hours. Repeated dose pharmacokinetics have not been studied.

Butorphanol is metabolized extensively in the liver and excreted in the urine. The volume of distribution is large, suggesting wide distribution into tissue.

### ***User Safety***

A user risk assessment was provided in compliance with the relevant guideline which shows that the product is not considered to present an unacceptable risk to the user, when used as recommended.

Warnings and precautions, as listed on the product literature, are adequate to ensure safety to users of the product. Therefore, the following applicant's user recommendations are appropriate:

- Butorphanol has opioid-like activity. The most frequent adverse effects of butorphanol in humans are drowsiness, sweating, nausea, dizziness, and vertigo and these may occur following unintended self-injection. Care should be taken to avoid accidental injection/self-injection. If accidental self-injection occurs, seek medical advice immediately and show the package leaflet or the label to the physician. Do not drive. An opioid antagonist (e.g. naloxone) may be used as an antidote.
- Wash splashes from skin and eyes immediately.

### ***Environmental Safety***

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

The applicant has provided a Phase I environmental risk assessment containing sufficient information to conclude that the assessment ends at Phase I, based on question 5 of the decision tree, as it will be used to treat a small number of animals in a flock or herd. As such environmental exposure will be low and a Phase II ERA was not required.

The product is not expected to pose a risk to the environment when used as recommended.

## ***III.B.2 Residues documentation***

### ***Residue Studies***

Due to the legal basis of the application, no new residues studies were conducted.

### ***Withdrawal Periods***

Due to the legal basis of the application, the same withdrawal periods as the reference products for horse meat and offal of zero days are justified. Milk from horses cannot be used for human consumption.

#### **IV. CLINICAL DOCUMENTATION**

As this is a generic application, and bioequivalence with the reference products has been established on the basis of essential similarity, efficacy studies are not required. The efficacy claims, dosing regimens, and pharmacology for this product are equivalent to those of the reference products.

#### **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 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](http://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](http://www.gov.uk/check-animal-medicine-licensed))