MINISTERIO
DE SANIDAD
Y POLÍTICA SOCIAL

agencia española de
medicamentos y
productos sanitarios

SUBDIRECCIÓN GENERAL
DE MEDICAMENTOS
DE USO VETERINARIO

Agencia Española de Medicamentos y Productos Sanitarios

Parque Empresarial Las Mercedes
Edificio 8
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28022 – Madrid
España

(Reference Member State)

MUTUAL RECOGNITIONPROCEDURE

DRAFT PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

B. Braun Vet Care Hartmann' s Lactated Ringers Solution for infusion for cattle, horses, sheep, goats, pigs, dogs and cats

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0153/001/MR
Name, strength and pharmaceutical form	CMS except DE and AT: B. Braun Vet Care Hartmann' s Lactated Ringers Solution for infusion for cattle, horses, sheep, goats, pigs, dogs and cats. (translated into the respective languages) DE and AT: Ringer-Lactat-Lösung nach Hartmann B. Braun Vet Care, Infusionslösung für Rinder, Pferde, Schafe, Ziegen, Schweine, Hunde und Katzen RMS: Lactato de Ringer Hartmann Braun solución para perfusión para bovino, equino, ovino, caprino, porcino, perros y gatos
Applicant	B. Braun Vet Care GmbH Am Aesculap-Platz D-78532 Tuttlingen Germany
Active substance(s)	Sodium chloride, potassium chloride, calcium chloride dihydrate, sodium (S- lactate)
ATC Vet code	QB05BB01
Target species	Cattle, horses, , sheep, goats, pigs, dogs and cats
Indication for use	Indication for all target animal species: -Isotonic dehydration -Metabolic acidosis -Hypotonic dehydration -Maintenance of normal extracellular fluid levels -Electrolyte replacement in burns

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies website (http://www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Mutual Recognition application in accordance with Article 13 a of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	23rd of March 2010
Date product first authorised in the Reference Member State (MRP only)	19th of November 2003
Concerned Member States for original procedure	AT, BE, DE, IE, IT, NL and UK

I. SCIENTIFIC OVERVIEW

***For public assessment reports for the first authorisation in a range**:*

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

II. QUALITY ASPECTS

A. Composition

100 ml of the product contains:

Active substances:	
Sodium chloride	0.600 g
Potassium chloride	0.040 g
Calcium chloride dihydrate	0.027 g
Sodium (S) - lactate	0.312 g
(as sodium lactate solution (50% w/v)	0.624 g)

Excipients:
Water for injections

The containers are low density polyethylene bottles of 500 and 1000 ml. A PE cap is incorporated to the closed bottle and sealed together. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation is justified.

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

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site.

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

C. Control of Starting Materials

The active substances are sodium chloride, potassium chloride, calcium chloride dihydrate and sodium lactate solution, established active substances described in the European Pharmacopoeia. The MAH confirms that the active substances are manufactured in accordance with the principles of good manufacturing practice.

The active substances specifications are considered adequate to control the quality of the materials. Batch analytical data demonstrating compliance with these specifications have been provided.

A certificate of suitability No. R1-CEP 1999-038-Rev 00 for sodium (S)-lactate solution is provided.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

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

E. Control on intermediate products

Not applicable.

F. 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.

G. Stability

The active substances are fully tested to ensure compliance with its specification immediately prior to its use in manufacture of the product.

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

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACOTOXICOLOGICAL)

This is an application according to Article 13a, well established veterinary use, and appropiate scientific literature about safety and residues tests was provided.

This veterinary medicinal product is a solution for injection by intravenous infusion that contains sodium chloride, potassium chloride, calcium chloride dihydrate and sodium (S)-lactate as active substances. It is indicated for isotonic dehydration, metabolic acidosis, hypotonic dehydration, maintenance of normal extracellular fluid levels and electrolyte replacement in burns.
The target species are horses, cattle, sheep, goats, pigs, dogs and cats.

III.A Safety Testing

Pharmacological Studies

The applicant has provided bibliographical data which show that the electrolytes Na+, K+, Ca2+, Cl- as well as the metabolisable anion lactate are indispensable for the maintenance and correction of fluid and electrolyte homeostasis and acid-base balance. All substrates are occurring during normal physiological metabolism.

The applicant has also provided bibliographical data which show that the bioavailability of the active substances is 100% because it is i.v. application. The metabolism of this veterinary medicinal product is that of each of its components: Na+, K+, Ca2+, Cl-, and lactate.

Toxicological Studies

The applicant has provided bibliographical data which show that the solution has low toxic potential and, at the recommended posology, it is not expected to cause any kind of genotoxicity and carcinogenicity.

The safety of the veterinary medicinal product has not been established during pregnancy and lactation so it will be only administered after risk/benefit evaluation by the responsible veterinarian.

User Safety

The applicant has provided a user safety assessment which shows that the risk for the professional user is acceptable when the product is used in accordance with label recommendations.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that the product does not pose a risk to the environment when it is used in accordance with label recommendations.

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

III.B Residues documentation

Residue Studies

No residue depletion studies were conducted because the active substances of the product are included in Annex II of Council Regulation 470/2009, are natural substances and are normal components of the diet of animals. The amount of these active substances in the body following therapeutic treatment of food-producing animals with this product would be indistinguishable from those naturally occurring in the animal.

MRLs

Active substances are listed in Annex II of Council Regulation 470/2009 for all food-producing species.

Withdrawal Periods

Based on the data provided above, a withdrawal period of zero days for meat and offal, and zero hours for milk is justified.

IV. CLINICAL ASSESSMENT (EFFICACY)

In many different clinical conditions, e.g. diarrhoea, vomiting, blood loss, burns, fistulas and fever, marked fluid and electrolyte losses can become a severe hazard for the patient and parenteral rehydration may become necessary.

According to the SPC this veterinary medicinal product is intended to be used in cattle, horse, sheep, goat, pig, dog and cat for isotonic dehydration, metabolic acidosis, hypotonic dehydration, maintenance of normal extracellular fluid levels and electrolyte replacement in burns.

IV.A Pre-Clinical Studies (pharmaceuticals only)

The applicant has provided bibliographical data that show that since electrolytes and lactate contained in this veterinary medicinal product are physiologically occurring substrates in animal body, in general, they follow the physiological pathways of the organism. All constituents used in this veterinary medicinal product are physiological constituents of the blood; their physiological pathways in the body are well known and are described in detail in the literature.

Tolerance in the Target Species of Animals

It is obvious that all possible adverse drug reactions (ADR) related to isotonic electrolyte solutions with metabolisable anions (i.e. lactate) are due to overdose and excess. With unimpaired renal function, adequate monitoring and following the recommended dosage for this veterinary medicinal product, no excess should be expected since the electrolyte concentrations in the product are within the range of the physiological serum concentrations. However, in case overdose has occurred the rate of infusion should be drastically reduced or the infusion should be stopped.

Local Tolerance

The product contains electrolytes and lactate in concentration comparable to the concentration which can generally be considered as safe in target species infusion therapy. Thus, no adverse effects on local tolerance have to be expected during or after administration.

IV.B Clinical Studies (pharmaceuticals and immunologicals)

Laboratory Trials

No studies were conducted with the product, however, LR is frequently used in rehydration therapy in target species and decades of experience have shown that the administration of solutions like this product is efficacious and safe.

Field Trials

The applicant provided bibliographical data which show that this veterinary medicinal product is one of the options to use for reversing hypovolaemia. This product contains

approximately the same concentration of electrolytes as serum. It is therefore a safe fluid to use if electrolytes cannot be measured.

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 risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

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 veterinary Heads of Agencies website (www.hma.eu).

This section 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.

None