IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Vetivex 11 (Hartmann's) solution for infusion for cattle, horses, dogs and cats

PRODUCT SUMMARY

EU Procedure Number	UK/V/0457/001, UK/V/0458/001
Name, Strength, Pharmaceutical Form	Vetivex 11 (Hartmann's) solution for infusion for cattle, horses, dogs and cats
Active Substances(s)	Sodium lactate ,Sodium chloride ,Potassium chloride,Calcium chloride
Applicant	Dechra Regulatory B.V., Handelsweg 25, 5531 AE Bladel, Netherlands
Legal Basis of Application	Generic application (Article 13(1) of Directive No 2001/82/EC)
Target Species	Cats,Cattle,Dogs,Horses
Indication For Use	This product is administered by intravenous infusion for the treatment of dehydration and metabolic acidosis in cattle, horses, dogs and cats. It may be used to correct volume depletion (hypovolaemia) resulting from gastrointestinal disease or shock.
ATC Code	QB05BB01
Date of completion of the original decentralised procedure	24 April 2013 (UK) 09 August 2013 (IE)
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Belgium, Denmark, France, Germany, Ireland (now RMS), The Netherlands, Luxembourg, Sweden UK added via RMS change

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.
The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

I. SCIENTIFIC OVERVIEW

This was an application for a generic product in accordance with Article 13 (1) of Directive 2001/82/EC as amended, for Vetivex 11 (also known as Hartmann's) Solution for Infusion for Cattle, Horses, Dogs and Cats, for which the reference product was Isolec Solution for Injection. The product is indicated for use in cattle, horses, dogs and cats, for the treatment of dehydration and metabolic acidosis. It may also be used following shock or gastrointestinal disease to correct hypovolaemia, (water depletion).

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 slight reactions observed are indicated in the SPC. The product is safe for the user, the consumer of foodstuffs from treated animals (horses, cattle), 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

The product contains sodium lactate 3.17 ml/ml, sodium chloride 6 mg/ml, potassium chloride 0.40 mg/ml and calcium chloride 0.20 mg/ml, equivalent to calcium chloride dehydrate 0.27 mg/ml. The solution is equivalent to 131 mmol/litre sodium, 5 mmol/litre potassium, 2 mmol/litre calcium, 29 mmol/litre bicarbonate (as lactate) and 111 mmol/litre chloride. The excipients are water for injections and hydrochloric acid, dilute, (for adjustment of pH).

The container/closure system consists of a polyvinylchloride infusion bag overwrapped with polypropylene. There are two ports on each pack size, with a combi port presented on the 5000ml combi pack. Two 5000 ml bags can be connected enabling the administration of volumes in excess of 5000 ml to be administered during one infusion if required. Pack sizes are 250 ml, 500 ml, 1000 ml, 3000 ml, 5000 ml and the 5000 ml combi or boxes containing 20 x 250 ml, 20 x 500 ml, 10 x 1000 ml, 4 x 3000 ml, 2 x 5000 ml, 2 x 5000 ml combi.

The particulars of the containers and controls performed are provided and conform to the regulation. The absence of preservative has been 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 in batches of 10,000 litres.

Process validation data on the product have been presented in accordance with the relevant European guidelines. The salts are dissolved into water, before being made up to solution and pH tested. The product is filtered and placed into the bags, with microbiological analysis and sterilisation by autoclave. The contents are tested for identity of the salts, and impurities, and the pH adjusted if necessary. Batch analysis from three pilot scale batches of the 500 ml product were analysed.

C. Control of Starting Materials

The active substances are sodium lactate, sodium chloride, potassium chloride and calcium chloride, established active substances described in the European Pharmacopoeia (Ph. Eur). Active substance specifications and Ph. Eur. Certificates of Suitability have been provided for the active substance manufacturers. The active substances are manufactured in accordance with the principles of good manufacturing practice.

The active substance specifications are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided. Water for injections used in the product adheres to the relevant Ph. Eur monograph, as does the hydrochloric acid included.

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. Tests include those for identification of active substances, contamination, endotoxins, integrity of packaging, fill volume and frangibility.

G. Stability

Stability test were not performed on the active substances, but as these are established active substances, no tests were required. Product was stored at 25^{o}C/ 60% RH for twenty-four months (one batch for eighteen months), and 40^{o}C for six months using the pack sizes to be marketed. All components were tested at various time points. A loss of weight due to moisture permeation may be evident, but this is noted by the inclusion of relevant instructions in the SPC.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
The product should be used immediately and not stored after opening.

Do not store above 25°C.
Do not freeze.

III SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a generic application according to Article 13, and bioequivalence with a reference product has been successfully claimed, results of pharmacological and toxicological tests are not required. These aspects of this product are considered to be identical to the reference product.
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 Testing

User Safety

The applicant has provided a user safety assessment in compliance with the relevant guideline which showed the following:-

Sodium chloride

Sodium chloride is considered the most important salt for maintaining correct osmotic tension, with between 5-12 g per day being considered normal consumption in the diet. Although in general considered a non-irritant and non-toxic substance, high levels can induce irritation of the gastro-intestinal tract, hypertraemia, vomiting, convulsions or death. Sodium chloride is neither an eye irritant or skin sensitiser.

Sodium lactate

Sodium lactate is commonly used in food products, cosmetics and human and veterinary medicines, and is a physiological salt found in the body. In general, sodium lactate is considered non-toxic or non-irritant, but large amounts should be avoided.

Potassium chloride

The safety of potassium chloride is well-established the substance is commonly used in medicinal products. Large amounts of this substance when ingested may cause gastro-intestinal tract irritation, vomiting, nausea and diarrhoea. If given parenterally, rapid injection of a high dose of potassium chloride can cause cardiac arrest.

Calcium chloride dehydrate

This commonly used substance is moderately toxic via ingestion, and may cause heart or stomach dysfunction.
The product will be administered by a veterinarian, and ocular or dermal exposure are unlikely, due to the nature of the packaging. Appropriate user warnings are included in the SPC.
For all substances, warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Ecotoxicity

The applicant provided a Phase I environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was required. The assessment concluded that as the product is to be used in a small number of individual target animals, the Environmental Risk Assessment may stop at Phase I. 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

No residues data were submitted. This was considered acceptable because the active substances fall under the justification for omission of this data based on well-established use and the confirmation of bioequivalence, by virtue of the fact that the product is administered via the same means as the reference product. Sodium chloride does not require maximum resides level data according to Table 1 of the Annex to Commission Regulation 37/2010.

Withdrawal Periods

Based on the data provided above, a withdrawal period of zero days for meat and offal and zero hours for milk were established for cattle and horses.

IV. CLINICAL ASSESSMENT

As this is a generic application according to Article 13, and bioequivalence with a reference product has been demonstrated, efficacy studies are not required. The efficacy claims for this product are equivalent to those of the reference product.

IV.A Pre-Clinical Studies

Pharmacology

As this was a generic application and bioequivalence was successfully claimed with a reference product, no data were required in this section.

Tolerance in the Target Species of Animals

As this was a generic application and bioequivalence was successfully claimed with a reference product, no data were required in this section.

IV.B Clinical Studies

As this was a generic application and bioequivalence was successfully claimed with a reference product, no data were required in this section.

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 for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable