Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

DIVENCE IBR MARKER LIVE Lyophilisate and Solvent for Emulsion for Injection

Date Created: January 2025

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	DIVENCE IBR MARKER LIVE Lyophilisate and Solvent for Emulsion for Injection
Applicant	Laboratorios Hipra SA, Avda La Selva 135, 17170 Amer (Girona), Spain
Active substance(s)	Live gE- tk- double-gene deleted Infectious Bovine Rhinotracheitis Virus (BoHV-1), strain CEDDEL
ATC Vetcode	QI02AD01
Target species	Cattle
Indication for use	Active immunisation of cattle from 10 weeks of age to reduce virus shedding, hyperthermia and clinical signs of IBR (infectious bovine rhinotracheitis).

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	Full application in accordance with Article 8 of VMRs 2013 (Schedule 1, Part 1) as amended.
Date of conclusion of the procedure	14/10/24

I. SCIENTIFIC OVERVIEW

This is a full application for Divence IBR Marker Live which contains live genetically modified bovine herpesvirus 1 which is already authorised in Great Britain.

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, 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 [2] of the product was demonstrated 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 live gE- tk- double-gene deleted Infectious Bovine Rhinotracheitis Virus (IBRV), strain CEDDEL, the adjuvant montanide and the excipients dipotassium phosphate, gelatin, glycine, potassium dihydrogen phosphate, sorbitol, sucrose, disodium phosphate dodecahydrate, potassium chloride, potassium dihydrogen phosphate, sodium chloride and water for injections.

The container/closure system consists of type I glass or PET vials closed with rubber stoppers and aluminium caps. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the adjuvant and vaccine strain are justified.

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

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

II.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 regulatory guidelines.

II.C. Control of Starting Materials

The active substance is live gE- tk- double-gene deleted Infectious Bovine Rhinotracheitis Virus (IBRV), strain CEDDEL, an established active substance described in in-house monographs. The active substance is manufactured in accordance with the principles of good manufacturing practice.

Starting materials of non-biological origin used in production comply with Ph. Eur.

Biological starting materials used are in compliance with the relevant Ph. Eur. Monographs and guidelines and are appropriately screened for the absence of extraneous agents according to the Ph. Eur.; any deviation was adequately justified.

The master and working seeds have been produced according to the Seed Lot System as described in the relevant guideline.

II.C.4. Substances of Biological Origin

Scientific data and/or certificates of suitability issued by the EDQM have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

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

The tests performed during production are described and the results of 3 consecutive runs, conforming to the specifications, are provided.

II.E. Control Tests on the Finished Product

The tests performed on the final product conform to the relevant requirements; any deviation from these requirements is justified.

The demonstration of the batch to batch consistency is based on the results of six batches produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

II.F. Stability

The active substance is 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 regulatory guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

The in-use shelf-life of the reconstituted vaccine is supported by the data provided.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 18 months.
Shelf life of the solvent as packaged for sale: 3 years.
Shelf life after reconstitution according to directions: 2 hours.
Store and transport refrigerated (2 ºC - 8 ºC).
Do not freeze.
Protect from light.

III. SAFETY ASSESSMENT

Laboratory trials

The safety of the administration of one dose, an overdose and the repeated administration of one dose in the target animal is demonstrated. The investigation was performed according to the recommendations of VMRs 2013 (Schedule 1, Part 1) as amended and the relevant guidelines.

Effects on reproductive performance were examined. The study results showed no negative effects of vaccination on the outcome of pregnancy. It was determined that the vaccine can be used during lactation.

There are no data suggesting that this product might adversely affect the immune system of the vaccinated animal or its progeny therefore a specific study was not carried out.

Specific studies were carried out to describe the spread, dissemination, reversion to virulence, biological properties, recombination or genetic reassortment of the vaccine strain. The studies determined that the vaccine does not spread to the unvaccinated target species and the vaccine virus does not disseminate in the body tissues of the target animal. The vaccine was also shown to be negligible for reversion to virulence.

The adjuvant and excipients used are not within the scope of MRLs. Based on this information, no withdrawal period is proposed.

No specific assessment of the interaction of this product with other medicinal products was made. Therefore, an appropriate warning in the SPC is included.

Field studies

The applicant has provided two field studies to support safety of Divence in the field. Two multi-centre, randomised, double blinded and placebo controlled clinical trials investigating safety and efficacy were conducted. It was concluded that the vaccine is safe for use in the target species.

Ecotoxicity

The applicant provided a Phase 1 environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. No warnings are therefore required.

IV. CLINICAL ASSESSMENT (EFFICACY)

Clinical Studies

Laboratory Trials

The efficacy of the product has been demonstrated in laboratory studies in accordance with the relevant requirements.

A serological equivalence study was carried out, where animals were vaccinated with either Divence Penta, or other DIVENCE vaccines, with Divence IBR being the monovalent vaccine. Four laboratory challenge studies have been provided in support of Divence IBR, including onset and duration of immunity.

Onset of immunity was determined to be 3 weeks after completion of the basic vaccination scheme.

Duration of immunity was determined to be 6 months after completion of the basic vaccination scheme or 1 year after the completion of the re-vaccination scheme.

Field Trials

Two GCP, blinded field trials were presented. The studies did not present any relevant data for efficacy; however, it was determined that the use of the vaccine reduces virus shedding, hyperthermia and clinical signs of infectious bovine rhinotracheitis.

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)

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.

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