MINISTERIO
DE SANIDAD, SERVICIOS SOCIALES
E IGUALDAD

agencia española de
medicamentos y
productos sanitarios

DEPARTAMENTO DE
MEDICAMENTOS
VETERINARIOS

Agencia Española de Medicamentos y Productos Sanitarios

C/Campezo 1, Edificio 8
28022 – Madrid
España
(Reference Member State)

MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

GUDAIR

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	ES/V/0210/001/MR
Name, strength and pharmaceutical form	GUDAIR ≥ 2 mm ITT avian PPD emulsion for injection
Applicant	CZ Veterinaria, S.A. La Relva s/n Torneiros 36400 Porriño (Pontevedra) Spain
Active substance(s)	*Mycobaterium paratuberculosis* inactivate, strain 316F
ATC Vet code	QI04AB09 and QI03AB01
Target species	Sheep and goats
Indication for use	Active immunisation of sheep and goats to reduce clinical signs, lesions and mortality caused by M. paratuberculosis. It also reduces *M. paratuberculosis* faecal shedding in sheep.

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 12(3) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	Day 90: 25/09/2013
Date product first authorised in the Reference Member State (MRP only)	02/02/1994
Concerned Member States for original procedure	IS, NO

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 reactions observed are indicated in the SPC.
The product is safe for the user, and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC because this vaccine contains mineral oil.
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:

Active substance:

Mycobaterium paratuberculosis inactivate, strain 316F ……≥ 2 mm ITT avian PPD*

* Increase in skin thickness by ITT test in sheep with avian PPD compared to the bovine PPD

Adjuvants:
Mineral oil (Marcol 52)
Montanide 103
Montane 80

Excipient:
Thiomersal

The containers are glass vials Type II, 30 cc, containing 30 doses, with nitrile rubber stopper and aluminium seal. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the adjuvant, the vaccine strain, the inactivating agent and the presence of preservative are justified.

The inactivation process and the detection limit of the control of inactivation are correctly validated.

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.

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

C. Control of Starting Materials

Starting materials of non-biological origin used in production comply with European pharmacopoeia monographs and in-house specifications.

Biological starting materials used are in compliance with the relevant Ph. Eur. Monographs and guidelines.

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

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.

However, dossier includes risk assessment on the seed *Mycobacterium*, one starting material of animal origin. Date of isolation, inert passes through cell, no animal component, dilution factor and route of administration lead to the conclusion that there is not potential risk of transmission of TSEs.

E. Control tests during production

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

The tests include purity and identity, inactivation, sterility, dry weight and determination of thiomersal.

F. 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 tests include in particular fill volume, appearance, conductivity, viscosity, sterility, safety and batch potency.

The demonstration of the batch to batch consistency is based on the results of 3 batches produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

G. Stability

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. Satisfactory data have been provided to justify a shelf life of 2 years at 2-8°C for the storage of the vaccine.

The in-use shelf-life of the broached vaccine is supported by the data provided that determined to be used inmedatly.

III. SAFETY ASSESSMENT

Field studies

As indicated at Guideline on Data requirements for Immunological veterinary medicinal products intended for minor use or minor species/limited markets (EMA/CVMP/IWP/123243/2006-Rev.2), the field estudies can cover safety and efficacy in one trial.

In the next point (Efficacy) the assessment of the 5-year field trial carried out in Australian sheep, where the safety was also assessed, revealed that in nearly 50% of cases at 2 months p.v. animals had lesions at the injection site and in 20-25% of cases persisted for at least 4 years. As indicated, this information is included at the SPC.

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.B Clinical Studies)

Laboratory Trials

The applicant provides the following summary of three laboratory trials.

Reference test	Nº animals	Age	Results
LTS-2-1992 Sheeps Subcutaneous route	16	> 1 month	- Humoral and specific cellular response at 21 days p.v. - Positive result at ITT with avian PDD at 300 days p.v. - Positive result at γ-IFN (ELISA) until 150 days p.v. (some animals) - Positive humoral response (AGID test) until 150 days p.v.
LTG-1-1992 Goats Subcutaneous route	16	> 1 month	- Specific cellular response at 21 days p.v. Humoral response only in some animals - Positive result at ITT with avian PDD at 300 days p.v. - Positive result at γ-IFN (ELISA) until 150 days p.v. (some animals) - Positive humoral response (AGID test) until 150 days p.v.
"Paratuberculosis in sheep modifies and limits the development of the lesions (1996)"	8 pairs of twin lambs	15 days	Challenge: oral infection at 50 days p.v. and a second one at 270 days p.v.: - Control animals showed spread of granulomatous lesions to other regions of the intestinal wall. - Vaccinated animals showed only regressive granulomas limited to lymphoid tissues

Field Trials

Firstly, the applicant provides a summary of a field trial in Spain with 88 sheeps, 57 goats and 9 pairs of twin lambs. From this trial it is concluded:
- There were not significative differences in body weight between control and vaccinated animals at 15, 30 and 60 days p.v.
- Positive humoral response (AGID/ELISA) in almost all animals at 30 days p.v.
- Positive cellular response (γ-IFN and ITT) in all animals at 100 days p.v.

The applicant provides another field evaluation of OJD (Ovine Johne's Disease or Paratuberculosis of sheep caused by *Mycobacterium paratuberculosis*). It's a 5-year field trial carried out in Australian sheep, breed merino, from 1999 until 2004. In farms with OJD seroprevalence and losses due to this patology, 200 merino lambs were vaccinated with Gudair and 200 lambs with saline (placebo). The study concludes that in flocks, with a high prevalence of OJD, vaccination with Gudair stimulated specific immune responses and significantly reduced and delayed both OJD-related mortality and clinical signs and the excretion of *M. paratuberculosis* at faeces.

The applicant also includes scientific publications references about vaccination against ovine paratuberculosis.

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