College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

FIXR Clostri suspension for injection for cattle, sheep and goat

Created: November 2024

PRODUCT SUMMARY

EU procedure number	N/A
Name and pharmaceutical form	FIXR Clostri suspension for injection
Applicant	Kernfarm B.V. De Corridor 14D 3621 ZB Breukelen The Netherlands
Active substance(s)	Each 2 mL of the vaccine contains: α toxoid of *C. perfringens* Type A ≥ 0.3 IU* ß toxoid *of C. perfringens* Type C ≥ 10 IU* ε toxoid of *C. perfringens* Type D ≥ 5 IU* α toxoid of *C. septicum* ≥ 2.5 IU* α toxoid of *C. novyi* Type B ≥ 3.5 IU* Toxoid of *C. sordellii* 100% protection** Inactivated *C. chauvoei* 100% protection** * IU: International units of antitoxin per mL of rabbit serum. **Level of protection in guinea pigs (according to Ph. Eur.).
ATC vetcode	QI02AB01 (Cattle) / QI04AB01 (Sheep) / QI03AB (Goat)
Target species	Cattle, sheep, goat.
Indication for use	For the active and passive immunisation of cattle, sheep and goat against blackleg, infectious necrotic hepatitis, malignant oedema and enterotoxaemias caused by C. chauvoei, C. novyi Type B, C. septicum, C. sordellii and C. perfringens Types A, C and D. It also provides immunity against C. perfringens Type B, due to the combination of fractions of Type C (β toxin) and Type D (toxin). Onset of immunity: In goats: three weeks after completion of the basic vaccination. Has not been demonstrated in sheep and cattle. Duration of immunity: Has not been demonstrated.

PRODUCT INFORMATION

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this immunological veterinary medicinal product (IVMP) are available in the Union Product Database (UPD).

SUMMARY OF ASSESSMENT

Legal basis of original application	Generic application in accordance with Article 18 of Regulation (EC) 2019/6 as amended.
Date of completion of the original **national** procedure	24 October 2024
Date immunological veterinary medicinal product first authorised in the Reference Member State (MRP only)	N/A
Concerned Member States (CMS) for original procedure	N/A
CMS for subsequent use procedure	N/A
Withdrawn CMS during original mutual recognition procedure	N/A

1. SCIENTIFIC OVERVIEW

The IVMP is manufactured and controlled using validated methods and tests that ensure the consistency of the IVMP released on the market. This is a generic application according to Article 18, which is identical to a reference product CUBOLAC POLICLOSTRIDIAL 7/11, which has been authorised since 7 October 1997 in Spain.

The IVMP can be safely used in the target species; the slight reactions observed are indicated in the SPC.

The IVMP is also 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 IVMP was demonstrated according to the claims made in the SPC.

The overall risk/benefit analysis is in favour of granting a marketing authorisation for this IVMP.

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

2.A. Product description

The IVMP contains per 2 ml the following active substances:

α toxoid of *C. perfringens* Type A	≥ 0.3 IU*
ß toxoid *of C. perfringens* Type C	≥ 10 IU*
ε toxoid of *C. perfringens* Type D	≥ 5 IU*
α toxoid of *C. septicum*	≥ 2.5 IU*
α toxoid of *C. novyi* Type B	≥ 3.5 IU*
Toxoid of *C. sordellii*	100% protection**
Inactivated *C. chauvoei*	100% protection**

* IU: International units of antitoxin per mL of rabbit serum.
**Level of protection in guinea pigs (according to Ph. Eur.).

2.8 mg aluminium hydroxide (Al^{+3}) per 2 ml vaccine is included as adjuvant and the product contains also the excipients thiomersal as a preservative and water for injections.

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

The container/closure system consists of high density polyethylene vials of 100 mL and 250 mL with perforable butyl rubber stopper and aluminium seal.

The choice of the adjuvant, vaccine strains and presence of a preservative is justified.

2.B. Description of the manufacturing method

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

The product is manufactured in accordance with the European Pharmacopoeia (Ph. Eur.) and relevant European guidelines.

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

2.C. Production and control of starting materials

The active substances are established active substances described in the European Pharmacopeia.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification are provided.

A risk assessment was provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products was satisfactorily demonstrated.

Starting materials of non-biological origin used in production comply with in-house specifications.

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.

The master and working seeds were produced according to the seed lot system as described in the relevant guideline(s).

2.D. Control tests during the manufacturing process

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

In-process control tests are carried out on intermediate stages of manufacture in order to verify the consistency of the manufacturing process and the final IVMP.

A specification was set for each intermediate and the analytical methods are described and validated, if applicable.

A shelf life and storage conditions for the intermediate IVMP are defined based on data resulting from stability studies.

2.E. Control tests on the finished product

For all tests, a short description of the techniques for analysing the finished product is provided. The tests and their specifications and limits are justified and are considered appropriate to adequately control the quality of the IVMP.

Satisfactory validation data for each analytical methods are provided, if appropriate.

The tests performed on the final product conform to the relevant requirements and monographs, if applicable; any deviation from these requirements is justified.

Batch analytical data from the proposed production site(s) are provided demonstrating compliance with the determined specification.

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.

2.F. Batch-to-batch consistency

Full protocols of 3 consecutive batches of the product, representative of the routine production and giving the results for all tests performed during production and on the finished product, are provided in order to ensure that quality is consistent from batch to batch and to demonstrate conformity with the predefined specifications.

2.G. Stability tests

Stability data on the active substance(s) are provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

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

3. SAFETY DOCUMENTATION (safety and residues tests)

This is a generic application according to Article 18, which is identical to a reference product and relies on the results of the appropriate safety, residue, pre-clinical and clinical studies for this reference product.

Due to the legal base of the application, the applicant is not required to submit pharmacological and toxicological data. The applicant has not submitted these data on the basis that bioequivalence with the respective reference product has been demonstrated.

The applicant confirms that the biological veterinary medicinal product is identical to the reference biological veterinary product. The raw materials used and the manufacturing processes are the same. Therefore, no additional data has been provided on the safety and efficacy of the product, with the exception of an Environmental Risk Assessment.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure the safety of the product to users / the environment / consumers.

User safety

As the generic is identical to the reference product, the same user safety warnings as for the reference product are stated in the SPC. Users should avoid self-injection, as this may give rise to a nodule at the injection site. In case of accidental self-injection, the user should seek medical advice immediately.

Environmental Risk Assessment

The applicant provided an environmental risk assessment in compliance with the relevant guideline. The assessment concluded that the environmental risk for FIXR Clostri is neglectable. No warnings in the SPC are therefore required.

Withdrawal Periods

As the generic is identical to the reference product, a withdrawal period of zero days for meat and milk in cattle, sheep, goats is justified.

4. EFFICACY DOCUMENTATION

This is a generic application according to Article 18, which is identical to a reference product and relies on the results of the appropriate safety, residue, pre-clinical and clinical studies for this reference product.

Due to the legal base of the application, the applicant is not required to submit pre-clinical or clinical data. The applicant has not submitted these data on the basis that bioequivalence with the respective reference product has been demonstrated.

The applicant confirms that the biological veterinary medicinal product is identical to the reference biological veterinary product. The raw materials used and the manufacturing processes are the same. Therefore, no additional data shall be provided on the safety and efficacy of the product

5. 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 are acceptable.

POST-AUTHORISATION PROCEDURES

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/labelling/package leaflet is/are available in the Union Product Database (UPD).

This section contains information on significant changes agreed after the original procedure, which are important for the quality, safety or efficacy of the product.

Significant variations: None.

Summary of change (Application number)	**Approval date**