<Date>

Direct animal healthcare professional communication (DaHPC)

HIPRABOVIS IBR MARKER LIVE (Infectious bovine rhinotracheitis vaccine (live)) - Increase in the incidence of anaphylactic-type reactions in cattle

Dear Veterinarian,

Laboratorios HIPRA, S.A. in agreement with the European Medicines Agency and the <National Competent Authority>, would like to inform you of the following:

Summary

- Since early 2022, an increase in the incidence of anaphylactic-type reactions in cattle has been observed after the use of the vaccine HIPRABOVIS IBR MARKER LIVE.
- Within the period from 1 March 2022 to 31 May 2022, a total of 27 cases involving 175 animals that had an anaphylactic-type reaction, and 8 animals that have died, have been reported. In at least 5 of the animals that have died, the animals had anaphylactic-type reactions with a fatal outcome.
- Most of the cases have been reported in specific geographic regions of Spain (19/27) and Italy (7/27). Within this period, more than 641,075 doses have been administered in 14 EU countries. This situation has not been observed in other EU countries where the vaccine is currently used.
- In most cases several other vaccines had previously and/or concomitantly been administered to the animals.
- A clear root cause has not been identified yet and investigations are ongoing. The product information will be updated on the frequency and severity of hypersensitivity / anaphylactic-type reactions.
- Veterinarians are recommended to promptly report any adverse events observed to the <National Competent Authority> and HIPRA at the earliest opportunity. It is recommended to provide the complete vaccination history and overview of the products used to the reacting animals, where possible. This information will enable further evaluation of the issue.

Background on the issue/concern

HIPRABOVIS IBR MARKER LIVE was first authorised in January 2011. It consists of a live attenuated vaccine which includes a live gene-deleted Infectious Rhinotracheitis Virus, strain CEDDEL as the active ingredient. The CEDDEL strain used in the vaccine is a double deletion mutant, which. reduces the virulence of the vaccine strain and allows the differentiation of animals with antibodies to gE (infected) and those without (vaccinated). The vaccine is intended for the active immunisation of calves from 3 months of age and adult cows, to reduce clinical signs of infectious bovine rhinotracheitis (IBR) and field virus excretion.

Vaccination is the main approach for the management of Infectious Bovine Rhinotracheitis. The presence of eradication programs in some European (EU) countries makes the use of vaccines an important tool for protecting national herds

and as a trading tool once BoHV-1 has been eradicated in some countries. Furthermore, if eradication is one of the goals of vaccination, marker vaccines need to be used to allow monitoring of the herds.

Hypersensitivity reactions are adverse events already described in the product information of HIPRABOVIS IBR MARKER LIVE with a frequency of 'very rare'. The present letter is to inform you of an increase in the number of cases related to anaphylactic-type reactions, which has been observed in specific geographic areas of Spain and Italy. Within the period from 1 March 2022 to 31 May 2022, a total of 27 cases involving 175 animals that had an anaphylactic-type reaction, and 8 animals that have died, have been reported. Within this period, more than 641,075 doses have been administered in 14 EU countries. This situation has not been observed in other EU countries where the vaccine is currently used. In most cases several other vaccines had previously and/or concomitantly been administered to the animals.

A clear root cause has not been identified yet and investigations are currently ongoing. The product information will be updated on the frequency of hypersensitivity reactions from very rare to rare and on their severity with the addition of anaphylaxis (sometimes fatal). In case an anaphylactic-type reaction occurs, an appropriate symptomatic treatment should be administered.

Call for reporting

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Veterinarians are recommended to report any suspected adverse events via the national reporting system: <details on the national reporting system>). The complete vaccination history and overview of other veterinary medicinal products used previously in the reacting animals, whenever possible, including the product name(s) and batch details, should be also provided in the reports, if available. A questionnaire is available to the veterinarians upon request.

Company contact point:

Should you have any questions or require additional information, please contact us:

<Insert MAH contact details>

Topic-specific communication plan for: Direct animal health care professional communication (DaHPC) on the increase in the incidence of anaphylactic-type reactions in cattle after the use of HIPRABOVIS IBR MARKER LIVE	
Medicinal product / active substance	HIPRABOVIS IBR MARKER LIVE / Infectious bovine rhinotracheitis vaccine (live))
Marketing authorisation holder (MAH)	Laboratorios HIPRA, S.A.
Safety concern and purpose of the communication	Increase in the incidence of anaphylactic-type reactions in cattle after the use of the vaccine HIPRABOVIS IBR MARKER LIVE. The DaHPC intends to inform veterinarians of the observed increase in the incidence of anaphylactic-type reactions in cattle and encourage the reporting of such cases.
DaHPC recipients	Veterinarians. Details for each country to be discussed and agreed with the National Competent Authorities (NCAs) of the countries where HIPRABOVIS IBR MARKER LIVE is marketed.
Member States where the communication will be distributed	The communication will be disseminated in the European Economic Area (EEA) countries where HIPRABOVIS IBR MARKER LIVE is marketed.
Stakeholders to coordinate with	• European Medicines Agency (EMA) • National competent authorities of the EEA countries where HIPRABOVIS IBR MARKER LIVE is marketed • Veterinary associations in the EEA countries where HIPRABOVIS IBR MARKER LIVE is marketed
Means of dissemination	• Email • Post (via courier) • Publication on the MAH website (if applicable) • Publication on the EMA website • Publication on the websites of the national competent authorities of the countries where HIPRABOVIS IBR MARKER LIVE is marketed (where applicable)
Follow-up and measurement of effectiveness	• Acknowledgement of receipt from veterinarians • Feedback from veterinarians: comments, questions, etc. • Need for follow-up communication to be considered

Topic-specific communication plan for: Direct animal health care professional communication (DaHPC) on the increase in the incidence of anaphylactic-type reactions in cattle after the use of HIPRABOVIS IBR MARKER LIVE	
Timetable	**Date**
Preparation of draft DaHPC and draft communication plan (in English) by the MAH	11 July 2022
Submission of draft DaHPC and draft communication plan (in English) to EMA	11 July 2022
DaHPC and communication plan (in English) agreed by CVMP	14 July 2022
Submission of translated DaHPC to the national competent authorities (of the countries where HIPRABOVIS IBR MARKER LIVE is marketed) for review. **The communication plan and the DaHPC (in English) shall also be submitted accordingly.**	21 July 2022
Agreement of translations by national competent authorities of the countries where HIPRABOVIS IBR MARKER LIVE is marketed	28 July 2022
Dissemination of DaHPC	11 August 2022
Evaluation of effectiveness by the MAH	• By 11 September 2022: Rate of acknowledgement of receipt from veterinarians • By 30 September 2022: Number of comments and questions from veterinarians
Follow up required by the MAH	After 30 September 2022: Consider follow up communication on the basis of the rate of acknowledgement of receipt and the comments and questions received from veterinarians