ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

HIPRABOVIS IBR MARKER LIVE lyophilisate and solvent for suspension for injection for cattle.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 2 ml contains:

Lyophilisate:
Active substance:
Live gE^- tk^- double-gene deleted Bovine Herpes Virus type 1 (BoHV-1), strain CEDDEL: $10^{6.3}$ – $10^{7.3}$ $CCID_{50}$.

Abbreviations:
gE^-: deleted glycoprotein E; tk^-: deleted thymidine kinase; CCID: cell culture infectious dose

Solvent:
Phosphate buffer solution.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Lyophilisate and solvent for suspension for injection.

Lyophilisate: white to yellowish tablet.
Solvent: transparent homogenous liquid.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (calves and adult cows).

4.2 Indications for use, specifying the target species

For the active immunisation of cattle from 3 months of age against Bovine Herpes Virus type 1 (BoHV-1) to reduce the clinical signs of infectious bovine rhinotracheitis (IBR) and field virus excretion.

Onset of immunity: 21 days after completion of the basic vaccination scheme.
Duration of immunity: 6 months after completion of the basic vaccination scheme.

4.3 Contraindications

Do not use in case of hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings

None.

4.5 Special precautions for use

Special precautions for use in animals

Vaccinate healthy animals only.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

None.

4.6 Adverse reactions (frequency and seriousness)

A slight increase in body temperature up to 1° C is common within 4 days following vaccination. Occasionally, an increase in rectal temperature up to 1.63º C in adult cows and up to 2.18º C in calves may be observed. This transient rise in temperature is spontaneously resolved within 48 hours without treatment and it is not related to a febrile process.

A transient inflammation at the inoculation site is common in cattle within 72 hours post-vaccination. This slight swelling lasts for less than 24 hours in most cases.

Vaccination might exceptionally cause hypersensitivity reactions. In such cases, an appropriate symptomatic treatment should be administered.

4.7 Use during pregnancy, lactation or lay

Can be used during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

4.9 Amounts to be administered and administration route

Cattle: from the age of 3 months onwards.

Reconstitute the lyophilised tablet with the entire contents of the enclosed solvent to obtain a suspension for injection.

Recommended vaccination programme:

The recommended initial dose is 1 injection of 2 ml of the reconstituted vaccine per animal. The animal should be revaccinated 3 weeks later with the same dose.
Thereafter a single booster dose of 2 ml should be administered every six months.

The method of administration is by intramuscular route, in the neck muscles. The injections should be preferably administered on the alternate sides of the neck. The solvent should be allowed to warm to a temperature between 15 ºC to 20ºC before reconstitution of the lyophilised tablet. Shake well before use. Avoid the introduction of contamination during reconstitution and use. Use only sterile needles and syringes for administration.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

No adverse reactions except those mentioned in section 4.6 were observed after the administration of a 10-fold vaccine dose.

4.11 Withdrawal period(s)

Zero days.

5. IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: live bovine vaccines against IBR, ATCvet code: QI02AD01.

To stimulate active immunity against bovine herpesvirus type 1 (BoHV-1) in cattle. The vaccine contains a BoHV-1 strain (CEDDEL strain) that is double deleted within the genes coding for the gE surface protein and the tk enzyme. The tk deletion is related to reduced viral neurotropism andreduced establishment of latency. The absence of the gene coding for the gE surface protein entails that the vaccine does not elicit antibodies to glycoprotein E of BoHV-1 (marker vaccine). This enables discrimination between cattle vaccinated with this vaccine and cattle infected with BoHV-1 field virus or vaccinated with conventional non-marker BoHV-1 vaccines. Diagnostic tools designed to detect gE antibodies should be suitable for this purpose. Animals exposed to gE surface protein will test positive (eg cattle infected with BoHV-1 field virus or vaccinated with conventional non-marker BoHV-1 vaccines) but unexposed animals will test negative (ie non-infected animals, including those vaccinated with Hiprabovis IBR Marker Live). Animals vaccinated with Hiprabovis IBR Marker live will test positive (alongside cattle infected with BoHV-1 field virus or vaccinated with conventional non-marker BoHV-1 vaccines) when samples are analysed in tests based on the identification of antibodies to any other BoHV-1 antigens.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lyophilisate:
Disodium phosphate dodecahydrate
Potassium dihydrogen phosphate
Gelatine
Povidone
Monosodium glutamate
Sodium chloride
Potassium chloride
Sucrose
Water for injections

Solvent:
Disodium phosphate dodecahydrate
Potassium dihydrogen phosphate
Sodium chloride
Potassium chloride
Water for injections

6.2 Incompatibilities

Do not mix with any other veterinary medicinal product, except the solvent supplied for use with the veterinary medicinal product.

6.3 Shelf life

Shelf life of the lyophilisate as packaged for sale: 2 years.
Shelf life of the solvent as packaged for sale: 2 years.
Shelf life after reconstitution: 6 hours.

6.4 Special precautions for storage

Store and transport refrigerated (2° C - 8° C).
Do not freeze.
Keep the bottles in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

Lyophilisate: Colourless Type I glass bottle closed with a bromobutyl rubber closure and an aluminium cap.

Solvent: Colourless Type I glass bottle (10 ml) or Type II glass bottle (50 ml) closed with a bromobutyl rubber closure and an aluminium cap.

Package sizes:
Cardboard box containing 1 bottle with 5 doses of lyophilised tablet and 1 bottle with 10 ml of solvent.
Cardboard box containing 1 bottle with 25 doses lyophilised tablet and 1 bottle with 50 ml of solvent.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Laboratorios Hipra, S.A.
Avda. La Selva, 135
17170 Amer (Girona)
SPAIN
Tel. +34 972 43 06 60
Fax. +34 972 43 06 61
E-mail: hipra@hipra.com

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/10/114/001
EU/2/10/114/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

27/01/2011

10. DATE OF REVISION OF THE TEXT

27/01/2011

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu/.

PROHIBITION OF SALE, SUPPLY AND/OR USE

The import, sale, supply and/or use of this veterinary medicinal product is or may be prohibited in certain Member States on the whole or part of their territory pursuant to national animal health policy. Any person intending to import, sell, supply and/or use of HIPRABOVIS® IBR MARKER LIVE must consult the relevant Member State's Competent Authority on the current vaccination policies prior to the import, sale, supply and/or use.

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURING AUTHORISATION HOLDER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION REGARDING SUPPLY OR USE

C. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION WITH REGARD TO SAFE AND EFFECTIVE USE

D. STATEMENT OF THE MRLs

E. SPECIFIC OBLIGATIONS TO BE FULFILLED BY THE MARKETING AUTHORISATION HOLDER

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURING AUTHORISATION HOLDER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) of the biological active substance(s)

Laboratorios Hipra, S.A.
Avda. La Selva, 135
17170 Amer (Girona)
Spain

Name and address of the manufacturer(s) responsible for batch release

Laboratorios Hipra S.A.
Avda. La Selva, 135
17170 Amer (Girona)
Spain

B. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION REGARDING SUPPLY OR USE

To be supplied only on veterinary prescription.

According to Article 71 of Directive 2001/82/EC of the European Parliament and of the Council as amended, Member States prohibit or may prohibit the import, sale, supply and/or use of the veterinary medicinal product on the whole or part of their territory if it is established that:

a) the administration of the veterinary medicinal product to animals will interfere with the implementation of national programmes for the diagnosis, control and eradication of animal diseases, or will cause difficulties in certifying the absence of contamination in live animals or in foodstuffs or other products obtained from treated animals.

b) the disease to which the veterinary medicinal product is intended to confer immunity is largely absent from the territory.

C. CONDITIONS OR RESTRICTIONS OF THE MARKETING AUTHORISATION WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE PRODUCT

Not applicable.

D. STATEMENT OF THE MRLs

The active substance being a principle of biological origin intended to produce active immunity is not in the scope of Regulation (EC) 470/2009.

The excipients listed in section 6.1 of the SPC are either allowed substances for which Table 1 of the annex to Commission Regulation (EU) No 37/2010 indicates that no MRLs are required or are considered as not falling within the scope of Regulation (EC) No 470/2009 when used as in this product.

E. SPECIFIC OBLIGATIONS TO BE FULFILLED BY THE MARKETING AUTHORISATION HOLDER

The applicant should perform a specific test on the Master Seed Virus (MSV) and on the Georgia Bovine Kidney (GBK) cell lines that would detect growth of Brucella abortus, within 6 to 9 months post-authorisation.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARDBOARD BOX

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

HIPRABOVIS IBR MARKER LIVE lyophilisate and solvent for suspension for injection for cattle.

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each dose of 2 ml: Live gE^- tk^- double-gene deleted Bovine Herpes Virus type 1 (BoHV-1), strain CEDDEL: $10^{6.3} – 10^{7.3}$ $CCID_{50}$.

3. PHARMACEUTICAL FORM

Lyophilisate and solvent for suspension for injection.

4. PACKAGE SIZE

5 doses
25 doses

5. TARGET SPECIES

Cattle (calves and adult cows).

6. INDICATION(S)

For the active immunisation of cattle from 3 months of age against Bovine Herpes Virus type 1 (BoHV-1) to reduce the clinical signs of infectious bovine rhinotracheitis (IBR) and field virus excretion.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramuscular use, in the neck muscles.

Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal period: Zero days.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once reconstituted, use by 6 hours.

11. SPECIAL STORAGE CONDITIONS

Store and transport refrigerated (2 °C- 8 °C).
Do not freeze.
Keep the bottles in the outer carton in order to protect from light.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only - to be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Laboratorios Hipra, S.A.
Avda. La Selva, 135
17170 Amer (Girona)
SPAIN
Tel.+34 972 43 06 60
Fax.+34 972 43 06 61
E-mail: hipra@hipra.com

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/10/114/001
EU/2/10/114/002

17. MANUFACTURER'S BATCH NUMBER

Batch {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL FOR THE LYOPHILISATE

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

HIPRABOVIS IBR MARKER LIVE lyophilisate for suspension for injection for cattle.

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Each dose of 2 ml: Live gE^- tk^- double-gene deleted Bovine Herpes Virus type 1 (BoHV-1), strain CEDDEL: $10^{6.3} – 10^{7.3}$ $CCID_{50}$.

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

5 doses
25 doses

4. ROUTE(S) OF ADMINISTRATION

I.M.
To be reconstituted with the enclosed solvent.

5. WITHDRAWAL PERIOD

Withdrawal period: Zero days.

6. BATCH NUMBER

Batch{number}

7. EXPIRY DATE

EXP {month/year}
Once reconstituted, use by 6 hours.

8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

LABEL FOR THE SOLVENT

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Solvent for HIPRABOVIS IBR MARKER LIVE

2. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

10 ml.
50 ml

3. ROUTE(S) OF ADMINISTRATION

To be used for the reconstitution of the lyophilisate.

4. WITHDRAWAL PERIOD

Zero days

5. BATCH NUMBER

Batch {number}

6. EXPIRY DATE

EXP {month/year}
Once reconstituted, use by 6 hours.

7. THE WORDS "FOR ANIMAL TREATMENT ONLY"

B. PACKAGE LEAFLET

PACKAGE LEAFLET

HIPRABOVIS IBR MARKER LIVE

Lyophilisate and solvent for suspension for injection for cattle.

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer:

LABORATORIOS HIPRA, S.A.
Avda. La Selva, 135
17170 Amer (Girona)
SPAIN

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

HIPRABOVIS IBR MARKER LIVE lyophilisate and solvent for suspension for injection for cattle.

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Lyophilisate:
Each dose of 2 ml contains: Live gE^- tk^- double-gene deleted Bovine Herpes Virus type 1 (BoHV-1), strain CEDDEL: $10^{6.3} – 10^{7.3}$ $CCID_{50}$.

Abbreviations:
gE^-: deleted glycoprotein E; tk^-: deleted thymidine kinase; CCID: cell culture infectious dose

Solvent:
Phosphate buffer solution.

4. INDICATION(S)

For the active immunisation of cattle from 3 months of age against Bovine Herpes Virus type 1 (BoHV-1) to reduce the clinical signs of infectious bovine rhinotracheitis (IBR) and field virus excretion.

Vaccinated animals can be differentiated from field virus infected animals due to the marker deletion (gE^-) by means of commercial diagnostic kits, unless the animals were previously vaccinated with a conventional vaccine or infected with field virus.

Onset of immunity: 21 days after completion of the basic vaccination scheme.
Duration of immunity: 6 months after completion of the basic vaccination.

5. CONTRAINDICATIONS

Do not use in case of hypersensitivity to the active substance or to any of the excipients.

6. ADVERSE REACTIONS

A slight increase in body temperature up to 1°C is common within 4 days following vaccination. Occasionally, an increase in rectal temperature up to 1.63ºC in adult cows and up to 2.18º C in calves may be observed. This transient rise in temperature is spontaneously resolved within 48 hours without treatment and it is not related to a febrile process.

A transient inflammation at the inoculation site is common in cattle within 72 hours post-vaccination. This slight swelling lasts for less than 24 hours in most cases.

Vaccination might exceptionally cause hypersensitivity reactions. In such cases, an appropriate symptomatic treatment should be administered.

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Cattle (calves and adult cows).

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Cattle from the age of 3 months onwards: 2 ml/animal.
Intramuscular use, in the neck muscles.

9. ADVICE ON CORRECT ADMINISTRATION

Reconstitute the lyophilised tablet with the entire contents of the enclosed solvent to obtain a suspension for injection.

Recommended vaccination programme:

The recommended initial dose is 1 injection of 2 ml of the reconstituted vaccine per animal. The animal should be revaccinated 3 weeks later with the same dose. Thereafter a single booster dose of 2 ml should be administered every six months.

The method of administration is by intramuscular route, in the neck muscles. The injections should be preferably administered on the alternate sides of the neck. The solvent should be allowed to warm to a temperature between 15 to 20 ºC before reconstitution of the lyophilised tablet. Shake well before use. Avoid the introduction of contamination during reconstitution and use. Use only sterile needles and syringes for administration.

10. WITHDRAWAL PERIOD

Zero days.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.
Store and transport refrigerated (+2 °C to +8 °C). Do not freeze.
Keep the bottles in the outer cartonin order to protect from light.

Do not use after the expiry date (EXP) stated on the carton and the label.

Shelf-life after reconstitution according to directions: 6 hours.

12. SPECIAL WARNING(S)

- Can be used during pregnancy and lactation.
- Vaccinate healthy animals only.
- Apply the usual procedures for the handling of animals.
- Apply the usual aseptic procedures.
- No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.
- No adverse reactions except those mentioned in section were observed after the administration of a 10-fold vaccine dose.
- Do not mix with any other veterinary medicinal product, except the solvent supplied for use with the veterinary medicinal product.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

27/01/2011

Detailed information on this product is available on the website of the European Medicines Agency http://www.ema.europa.eu/.

15. OTHER INFORMATION

Pack sizes:

5 doses (lyophilisate and solvent)
25 doses (lyophilisate and solvent)

Not all pack sizes may be marketed.

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

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