SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

CZV BOVINE TUBERCULIN PPD, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose of 0.1 ml contains:

Active substance:
Purified protein derivative from culture of *Mycobacterium bovis*, strain AN-5..... 2,500 IU*
*IU: International units.

Excipients:
Phenol (preservative) .....0.5 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Transparent colourless or yellowish solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle

4.2 Indications for use, specifying the target species

In vivo diagnosis of cattle from 6 weeks of age that have generated an immune response against *Mycobacterium bovis*, the causative agent of bovine tuberculosis (single intradermal tuberculin test).

When used together with CZV Avian PPD Tuberculin, in vivo diagnosis of cattle from 6 weeks of age that have generated an immune response against *M. bovis*, differentiating animals reacting to *M. bovis* from those that have become sensitised to bovine tuberculin as a result of exposure to other mycobacteria or related genera (single intradermal comparative tuberculin test).

4.3 Contraindications

None.

4.4 Special warnings for each target species

It is not recommended to repeat the test until at least 42 days have passed since the previous test in order to avoid false negatives due to a loss of skin responsiveness during a period of post-test desensitisation.

When used in chronically infected animals with severe pathology, the tuberculin test may be unresponsive.

Newly infected animals may not react to the tuberculin test until the cell mediated immune response has developed (for most animals this is between 3–6 weeks post-infection).

Post-partum immunosuppression may give rise to false negative results in cattle that have recently calved.

A lack of sensitivity to the test can occur in cattle that were recently or concurrently treated with immunosuppressive agents.

4.5 Special precautions for use

Special precautions for use in animals

The results obtained with the test should be interpreted by taking into account other results obtained in the herd and the clinical and epidemiological factors which have led to the use of this test.

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

In case of accidental self-injection, persons who have been exposed to tuberculin protein, either from a previous tuberculosis vaccination, or from environmental exposure may develop a reaction within 48 to 72 hours, consisting of a skin reaction of a hard, dense wheal. Mild itching, swelling, or irritation at the site of the injection are frequent reactions. If a strong reaction or systemic symptoms occur, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases a transitory increase of the temperature up to a maximum of 41.4 ºC, within 3 days after injection, may be observed.

The frequency of adverse reactions is defined using the following convention:
- Very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment).
- Common (more than 1 but less than 10 animals in 100 animals).
- Uncommon (more than 1 but less than 10 animals in 1,000 animals).
- Rare (more than 1 but less than 10 animals in 10,000 animals).
- Very rare (less than 1 animal in 10,000 animals, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Although no specific laboratory safety tests were done in pregnant or lactating cattle, experience from field use indicate that the administration of CZV Bovine Tuberculin PPD does not have a negative effect on reproductive performance or lactation.

4.8 Interaction with other medicinal products and other forms of interaction

Safety and efficacy data are available which demonstrate that this immunological veterinary medicinal product can be administered on the same day but not mixed with CZV Avian Tuberculin PPD.

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

Care should be taken in the interpretation of tests carried out in cattle which have been previously vaccinated against bovine tuberculosis or Johne’s disease (paratuberculosis) because such vaccinations may cause false positive or false negative results in the tuberculin skin tests N.B.

Vaccination of cattle against bovine tuberculosis is currently forbidden in the EU. Vaccination of cattle against paratuberculosis may be forbidden in some EU Member States.

4.9 Amounts to be administered and administration route

Dose: 0.1 ml
Age of administration: from 6 weeks
Route of administration: intradermal

Administration Shake well before use.

Injection sites shall be clipped and cleansed. A fold of skin within each clipped area shall be taken between the forefinger and thumb and measured with callipers and recorded. The dose of CZV Bovine Tuberculin PPD shall then be injected intradermally into the deeper layers of the skin, in a defined area between the first and second third of the neck. A correct injection shall be confirmed by palpating a small pea-like swelling at each site of injection.

The distance between the two injections (CZV Bovine Tuberculin PPD and CZV Avian Tuberculin PPD) in the comparative intradermal test should be approximately 12–15 cm. In young animals in which there is no room to separate the sites sufficiently on one side of the neck, one injection must be made on each side of the neck at identical sites in the centre of the middle third of the neck.

The skin-fold thickness of each injection site shall be remeasured 72 ± 4 hours after injection and recorded.

Interpretation of the results

Single intradermal test

a) Positive: if it is observed an increase of 4 mm or more in the thickness of the fold of the skin at the injection site or clinical signs such as diffuse or extensive oedema, exudation, necrosis, pain or inflammation of the lymphatic ducts in that region or of the lymph nodes.

b) Inconclusive: if no clinical signs such as mentioned above are observed and if the increase in skin-fold thickness is more than 2 mm and less than 4 mm.

c) Negative: Increase of not more than 2 mm in the thickness of the fold of skin without clinical signs.

Animals inconclusive to the single intradermal test shall be subjected to another test after a minimum of 42 days.

Animals which are not negative to this second test shall be deemed to be positive to the test.

Animals positive to the single intradermal test may be subjected to an intradermal comparative test if false positive reaction or interference reaction is suspected.

Intradermal comparative test when CZV Bovine Tuberculin PPD and CZV Avian Tuberculin PPD are used together:

a) Positive: a positive bovine PPD reaction which is more than 4 mm greater than the avian reaction or the presence of clinical signs diffuse or extensive oedema, exudation, necrosis, pain or inflammation of the lymphatic ducts in that region or of the lymph nodes.

b) Inconclusive: a positive or inconclusive bovine PPD reaction which is from 1 to 4 mm greater than the avian reaction, and absence of clinical signs.

c) Negative: a negative bovine PPD reaction, or a positive or inconclusive bovine PPD reaction but which is equal to or less than a positive or inconclusive avian PPD reaction and the absence of clinical signs in both cases.

No other products except CZV Avian Tuberculin PPD should be administered before, at the same time or after the intradermal test near to the injection site.

Animals inconclusive to intradermal comparative test that are not removed as reactors by the competent authority shall be subjected to another test after a minimum of 42 days. Animals which are not negative to this second test shall be deemed positive to the test under EU legislation.

Different criteria for interpretation of results may be applied in accordance with national requirements for bovine tuberculosis eradication schemes

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

No local or systemic reactions other than those mentioned in section 4.6 are observed after administration of an overdose.

4.11 Withdrawal period

Zero days.

5. IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: immunologicals for Bovidae, in vivo diagnostic preparations for cattle.
ATCvet code: QI02AR01
In vivo diagnosis of the immune status of cattle against *Mycobacterium bovis*

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenol
Glycerine
Phosphate buffered saline:
- Sodium chloride,
- Disodium phosphate
- Potassium phosphate
Water for injections

6.2 Incompatibilities

Do not mix with any other veterinary medicinal product.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: use immediately.

6.4. Special precautions for storage

Store and transport refrigerated (2 º – 8 ºC).
Protect from light.
Do not freeze.

May be stored and transported up to a maximum of 37 ºC for a period not longer than 14 days.

6.5 Nature and composition of immediate packaging

Type I hydrolytic glass vials containing 50 doses (5 ml) with a rubber-butyl stopper and aluminium seal or colourless flip-off aluminium seal.
Type I hydrolytic glass vials containing 20 doses (2ml) with rubber-butyl stopper and aluminium seal or colourless flip-off aluminium seal.

Pack sizes:
Cardboard box of 1,250 doses with 25 vials of 5 ml.
Cardboard box of 500 doses with 10 vials of 5 ml
Cardboard box of 50 doses with 1 vial of 5 ml.
Cardboard box of 500 doses with 25 vials of 2 ml
Cardboard box of 200 doses with 10 vials of 2 ml
Cardboard box of 20 doses with 1 vial of 2 ml

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

CZ Vaccines S.A.U.
A Relva s/n – Torneiros
36410 O Porriño
Pontevedra
Spain

8. MARKETING AUTHORISATION NUMBER(S)

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9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25/10/1982
Renewal of the authorisation: 04/11/2016

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

The manufacture, import, possession, sale, supply and/or use of CZV Bovine Tuberculin PPD may be prohibited in certain Member State on the whole or part of its territory pursuant to national legislation. Any person intending to manufacture, import, possess, sell, supply and/or use CZV Bovine Tuberculin PPD must consult the relevant Member State's competent authority on the current policies prior to the manufacture, import, possession, sale, supply and/or use.

ANNEX III

LABELLING AND PACKAGE LEAFLET

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

CZV BOVINE TUBERCULIN PPD, solution for injection

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

One dose of 0.1 ml contains:
Purified protein derivative from culture of *Mycobacterium bovis*, strain AN-5 ..... 2,500 IU
Phenol.....0.5 mg

3. PHARMACEUTICAL FORM

Solution for injection

4. PACKAGE SIZE

5 ml
10 vials of 5 ml
25 vials of 5 ml
2 ml
10 vials of 2 ml
25 vial of 2 ml

5. TARGET SPECIES

Cattle

6. INDICATIONS

For *in vivo* diagnosis of bovine tuberculosis

7. METHOD AND ROUTES OF ADMINISTRATION

Intradermal use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal period: zero days.

9. SPECIAL WARNINGS, IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once opened, use immediately

11. SPECIAL STORAGE CONDITIONS

Store and transport refrigerated. Protect from light. Do not freeze.
May be stored and transported up to a maximum of 37 ºC for a period not longer than 14 days.

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 product 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.
The import, possession, sale, supply and/or use of this veterinary medicinal product may be prohibited in a Member State on the whole or part of its territory, see package leaflet for further information.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

CZ Vaccines S.A.U.
36410 O Porriño – Spain

16. MARKETING AUTHORISATION NUMBER(S)

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17. MANUFACTURER'S BATCH NUMBER

Batch {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial of 2 ml or 5 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

CZV BOVINE TUBERCULIN PPD

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Purified protein derivative from culture of *Mycobacterium bovis*, strain AN-5 ..... 2,500 IU/0.1 ml

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

2 ml (20 doses)
5 ml (50 doses)

4. ROUTES OF ADMINISTRATION

Intradermal use

5. WITHDRAWAL PERIOD(S)

Withdrawal period: zero days.

6. BATCH NUMBER

Batch {number}

7. EXPIRY DATE

EXP {months/year}
Once opened, use immediately

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

PACKAGE LEAFLET

PACKAGE LEAFLET
CZV BOVINE TUBERCULIN PPD, solution for injection

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 responsible for batch release:
CZ Vaccines S.A.U.
A Relva s/n – Torneiros
36410 O Porriño
Pontevedra
Spain

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

CZV BOVINE TUBERCULIN PPD, solution for injection

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

One dose of 0.1 ml contains:
Active substance:
Purified protein derivative from culture of *Mycobacterium bovis*, strain AN-5 ..... 2,500 IU*
*IU: International units.

Excipients:
Phenol (preservative) ..... 0.5 mg.

Transparent colourless or yellowish solution.

4. INDICATIONS

In vivo diagnosis of cattle from 6 weeks of age that have generated an immune response against *Mycobacterium bovis*, the causative agent of bovine tuberculosis (single intradermal tuberculin test).

When used together with CZV Avian PPD Tuberculin, in vivo diagnosis of cattle from 6 weeks of age that have generated an immune response against *M. bovis*, differentiating animals reacting to *M. bovis* from those that have become sensitised to bovine tuberculin as a result of exposure to other mycobacteria or related genera (single intradermal comparative tuberculin test).

5. CONTRAINDICATIONS

None.

6. ADVERSE REACTIONS

In very rare cases a transitory increase of the temperature up to a maximum of 41.4 ºC, within 3 days after injection, may be observed.

The frequency of adverse reactions is defined using the following convention:
- Very common (more than 1 in 10 animals displaying adverse reaction(s) during the course of one treatment).

- Common (more than 1 but less than 10 animals in 100 animals).
- Uncommon (more than 1 but less than 10 animals in 1,000 animals).
- Rare (more than 1 but less than 10 animals in 10,000 animals).
- Very rare (less than 1 animal in 10,000 animals, including isolated reports).

7. TARGET SPECIES

Cattle

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

Dose: 0.1 ml
Age of administration: from 6 weeks
Route of administration: intradermal

Administration Shake well before use.

Injection sites shall be clipped and cleansed. A fold of skin within each clipped area shall be taken between the forefinger and thumb and measured with callipers and recorded. The dose of tCZV Bovine Tuberculin PPD shall then be injected intradermally into the deeper layers of the skin, in a defined area between the first and second third of the neck. A correct injection shall be confirmed by palpating a small pea-like swelling at each site of injection.

The distance between the two injections (CZV Bovine Tuberculin PPD and CZV Avian Tuberculin PPD) in the comparative intradermal test should be approximately 12–15 cm. In young animals in which there is no room to separate the sites sufficiently on one side of the neck, one injection must be made on each side of the neck at identical sites in the centre of the middle third of the neck.

The skin-fold thickness of each injection site shall be remeasured 72 ± 4 hours after injection and recorded.

Interpretation of the results

Single intradermal test

a) Positive: if it is observed an increase of 4 mm or more in the thickness of the fold of the skin at the injection site or clinical signs such as diffuse or extensive oedema, exudation, necrosis, pain or inflammation of the lymphatic ducts in that region or of the lymph nodes.

b) Inconclusive: if no clinical signs such as mentioned above are observed and if the increase in skin-fold thickness is more than 2 mm and less than 4 mm.

c) Negative: Increase of not more than 2 mm in the thickness of the fold of skin without clinical signs.

Animals inconclusive to the single intradermal test shall be subjected to another test after a minimum of 42 days.

Animals which are not negative to this second test shall be deemed to be positive to the test.

Animals positive to the single intradermal test may be subjected to an intradermal comparative test if false positive reaction or interference reaction is suspected.

Intradermal comparative test when CZV Bovine Tuberculin PPD and CZV Avian Tuberculin PPD are used together:

a) Positive: a positive bovine PPD reaction which is more than 4 mm greater than the avian reaction or the presence of clinical signs diffuse or extensive oedema, exudation, necrosis, pain or inflammation of the lymphatic ducts in that region or of the lymph nodes.

b) Inconclusive: a positive or inconclusive bovine PPD reaction which is from 1 to 4 mm greater than the avian reaction, and absence of clinical signs.

c) Negative: a negative bovine PPD reaction, or a positive or inconclusive bovine PPD reaction but which is equal to or less than a positive or inconclusive avian PPD reaction and the absence of clinical signs in both cases.

No other products except CZV Avian Tuberculin PPD should be administered before, at the same time or after the intradermal test near to the injection site.

Animals inconclusive to intradermal comparative test that are not removed as reactors by the competent authority shall be subjected to another test after a minimum of 42 days. Animals which are not negative to this second test shall be deemed positive to the test under EU legislation.

Different criteria for interpretation of results may be applied in accordance with national requirements for bovine tuberculosis eradication schemes.

9. ADVICE ON CORRECT ADMINISTRATION

Shake well before use.

10. WITHDRAWAL PERIOD

Zero days.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Store and transport refrigerated (2 º – 8 ºC). Protect from light. Do not freeze.
May be stored and transported up to a maximum of 37 ºC for a period no longer than 14 days.

12. SPECIAL WARNINGS

Do not mix with any other veterinary medicinal product.

Special warnings for each target species:
It is not recommended to repeat the test until at least 42 days have passed since the previous test in order to avoid false negatives due to a loss of skin responsiveness during a period of post-test desensitisation.

When used in chronically infected animals with severe pathology, the tuberculin test may be unresponsive.

Newly infected animals may not react to the tuberculin test until the cell mediated immune response has developed (for most animals this is between 3–6 weeks post-infection).

Post-partum immunosuppression may give rise to false negative results in cattle that have recently calved.

A lack of sensitivity to the test can occur in cattle that were recently or concurrently treated with immunosuppressive agents.

Special precautions for use in animals:
The results obtained with the test should be interpreted by taking into account other results obtained in the herd and the clinical and epidemiological factors which have led to the use of this test.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
In case of accidental self injection persons who have been exposed to tuberculin protein, either from a previous tuberculosis vaccination or from environmental exposure may develop a reaction within 48 to 72 hours, consisting of a skin reaction of a hard, dense wheal. Mild itching, swelling, or irritation at the site of the injection are frequent reactions. If a strong reaction or systemic symptoms occur seek medical advice immediately and show the package leaflet or the label to the physician.

Use during pregnancy, lactation:
Although no specific laboratory safety tests were done in pregnant or lactating cattle, experience from field use indicate that the administration of CZV Bovine Tuberculin PPD does not have a negative effect on reproductive performance or lactation.

Interaction with other medicinal products and other forms of interaction:
Safety and efficacy data are available which demonstrate that this immunological veterinary medicinal product can be administered on the same day but not mixed with CZV Avian Tuberculin PPD.

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

Care should be taken in the interpretation of tests carried out in cattle which have been previously vaccinated against bovine tuberculosis or Johne's disease (paratuberculosis) because such vaccinations may cause false positive or false negative results in the tuberculin skin tests N.B. Vaccination of cattle against bovine tuberculosis is currently forbidden in the EU. Vaccination of cattle against paratuberculosis may be forbidden in some EU Member States.

Overdose (symptoms, emergency procedures, antidotes):
No local or systemic reactions other than those mentioned in section on "Adverse reactions" are observed after administration of an overdose.

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

Ask your veterinary surgeon how to dispose of medicines no longer required, These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Type I hydrolytic glass vials containing 50 doses (5 mL) and 20 doses (2 mL) with a rubber butyl stopper and aluminium seal or colourless flip-off aluminium seal.

Pack sizes
Cardboard box of 1,250 doses with 25 vials of 5 ml.
Cardboard box of 500 doses with 10 vials of 5 ml.
Cardboard box of 50 doses with 1 vial of 5 ml.
Cardboard box of 500 doses with 25 vials of 2 ml.
Cardboard box of 200 doses with 10 vials of 2 ml.
Cardboard box of 20 doses with 1 vial of 2 ml.

Not all pack sizes may be marketed.

The manufacture, import, possession, sale, supply and/or use of CZV Bovine Tuberculin PPD may be prohibited in certain Member State on the whole or part of its territory pursuant to national legislation. Any person intending to manufacture, import, possess, sell, supply and/or use CZV Bovine Tuberculin PPD must consult the relevant Member State's competent authority on the current policies prior to the manufacture, import, possession, sale, supply and/or use.