1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tuberculin PPD Kit

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Bovine Tuberculin PPD 3000:

Per 0.1 ml (1 dose):

Active substances:
Bovine Tuberculin purified protein derivative from culture of *Mycobacterium bovis*, strain AN5: 3000 IU*

Excipients:

Qualitative composition of excipients and other constituents
Phenol
Glucose anhydrous
Disodium phosphate dihydrate
Potassium dihydrogen phosphate
Water for injections

Avian Tuberculin PPD 2500:

Per 0.1 ml (1 dose):

Active substances:
Avian Tuberculin purified protein derivative from culture of *Mycobacterium avium* subspecies *avium*, strain D4ER: 2500 IU*

Excipients:

Qualitative composition of excipients and other constituents
Phenol
Glucose anhydrous
Disodium phosphate dihydrate
Potassium dihydrogen phosphate
Water for injections
Ponceau 4R (E124)

(*IU: International Units according to Ph. Eur.)

Solution for injection.
Bovine Tuberculin PPD 3000 is a clear, colourless to light yellow aqueous solution with a pH between 6.5 and 7.5. Avian Tuberculin PPD 2500 is a clear, red aqueous solution with a pH between 6.5 and 7.5.

3. CLINICAL INFORMATION

3.1 Target species

Cattle.

3.2 Indications for use for each target species

To be used for the *in vivo* identification of cattle which have been exposed to *Mycobacterium* species causing bovine tuberculosis. Simultaneous administration of Bovine Tuberculin PPD 3000 and Avian Tuberculin PPD 2500 in the Single Intradermal Comparative Cervical Tuberculin (SICCT) test enables differentiation between the specific delayed-type hypersensitivity reaction in cattle exposed to *Mycobacterium* species causing bovine tuberculosis and any non-specific reaction resulting from exposure to other species of mycobacteria or related genera, that induce sensitisation to Bovine Tuberculin PPD 3000.

3.3 Contraindications

None.

3.4 Special warnings

For an accurate SICCT test result the use of the veterinary medicinal product in cattle should be avoided within 42 days following a previous administration of tuberculin PPDs. It has been observed that a shorter interval between tests results in a potential loss of skin responsiveness and is therefore strongly discouraged.

The diagnostic accuracy of the test also depends upon the proper intradermal injection of the Bovine and Avian Tuberculin PPDs together with a meticulous measurement, characterisation, and comparison of the skin reactions 72 hours later. Subcutaneous (instead of intradermal) injection of tuberculin PPDs may give rise to an inaccurate test result and is also likely to lead to desensitisation of the animal for a variable period.

The accuracy of the test is also influenced by the site of injection of the tuberculin PPDs (see 3.9) and by the volume of each tuberculin PPD administered; doses less than the prescribed 0.1 ml will increase the risk of an inaccurate result of the SICCT test.

The sensitivity of the test can be influenced by concurrent infection with species of mycobacteria that do not cause bovine tuberculosis. The interval since infection with *Mycobacterium* species causing bovine tuberculosis, either where an immune response has not had sufficient time to develop, or where the immune response period has been superseded, can also impair the sensitivity of the SICCT test. Notice must be taken that the response is ordinarily somewhat depressed in the peri-parturient period. In the event of a fulminating or advanced infection leading to generalized tuberculosis, a response to the intradermal test can be depressed or even absent.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Not applicable.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
In case of accidental self-injection, persons sensitised to tuberculin, either from a previous tuberculosis vaccination, or from environmental exposure, may expect a local reaction. Over 48 to 72 hours this will cause a skin reaction of a hard, dense wheal. Mild itching, swelling, or irritation at the site of the

injection are frequent reactions in such persons. If a strong reaction or systemic symptoms develop, seek medical advice immediately and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:

Not applicable.

Other precautions:

Disease spread precautions.
Personal protective equipment consisting of suitable protective clothing and footwear should be worn when conducting tuberculin tests. All practicable measures of cleaning and disinfection of protective clothing, footwear, hands and equipment (syringes, etc.) should be undertaken on entry and exit from the holding to minimise the risk of disease transfer.

3.6 Adverse events

Target species: Cattle:

Very common (>1 animal / 10 animals treated):	Injection site swelling*
Uncommon (1 to 10 animals / 1 000 animals treated):	Elevated temperature**

* Shortly after administration, in particular in cattle infected with *Mycobacterium bovis.* In uninfected animals this swelling will greatly decrease in size within 24 hours and completely disappear within 3 to 4 days. In infected cattle and/or in cattle sensitised with non-specific mycobacteria the initial swelling will also decrease in size within 24 hours but it will take up to four weeks before it completely disappears.
** In infected cattle, will return to normal within 24 hours.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy, lactation and fertility:
Although no specific laboratory safety tests have been conducted in pregnant or lactating cattle, experience from field use indicate that the administration of Bovine and/or Avian Tuberculin PPD does not have a negative effect on reproductive performance or lactation.

3.8 Interaction with other medicinal products and other forms of interaction

Injection of other products at or adjacent to the site of tuberculin PPD injection should be avoided during the period immediately prior to tuberculin PPD injection and until the completion of the reading of the tuberculin test. Possible reactions due to such other products could be confused with, or otherwise affect, the delayed type hypersensitivity reaction elicited by the administration of tuberculin PPDs.

In general, it is recommended that no other veterinary medicinal product should be administered immediately before and after administration of Tuberculine PPD Kit.

In particular, the veterinary medicinal product should not be used in cattle which recently have been treated with immunosuppressive medicines such as glucocorticosteroids since such a treatment may influence the results of the tuberculin test.

A more severe interpretation of the tuberculin skin test may be required in animals vaccinated against Johne's Disease (paratuberculosis), as vaccination could give rise to false negative SICCT test results in such animals.

N.B. Vaccination of cattle against bovine tuberculosis is currently forbidden in the European Union.

Where administration of a medicinal product is unavoidable, such product should not be administered near the injection sites of Tuberculine PPD Kit and preferably applied on the opposite side of the neck or in another anatomical region.
Alternatively, consider deferring its administration until the responses to tuberculin PPDs have been read on the second day of the SICCT test.

3.9 Administration routes and dosage

Selection of sites of injection:
The approved injection sites are situated at the border of the anterior and middle thirds of either side of the neck. In adult animals the upper site (for Avian tuberculin PPD) is about four inches (10 cm) below the crest. The lower site (for Bovine tuberculin PPD) should be about five inches (12.5 cm) from the upper site, on a line drawn parallel with the line of the shoulder. In young animals where there is insufficient space to inject both tuberculin PPDs into the same side of the neck, the tuberculin PPDs should be injected, one on each side of the neck, at corresponding sites in the centre of the middle third of the neck. In animals with non-associated lumps or swellings near the injection site(s) the tuberculin PPD should be injected into the opposite side of the neck.

Preparation of sites of injection:
The selected sites of injection should be clipped (an adequately sized area for identification of the injection sites), cleansed (with water alone) if obviously dirty, and debris should be removed prior to injection. The presence of skin tuberculosis, any lumps or abnormalities near the tuberculin PPD injection site(s) should be recorded.

Measurement of skin thickness prior to the tuberculin injection:
Before injection, a fold of skin at each of the intended injection sites and within the clipped area must be taken between the forefinger and thumb and accurately measured to the nearest millimetre using callipers.

Intradermal injection:
A correct intradermal injection technique and the delivery of the prescribed dose volume of 0.1 ml per injection are important for a reliable test result. A correct injection is confirmed by palpating a small pea-like swelling at each injection site. If there is any doubt about either of the injections being delivered intradermally, a further injection should be made, preferably at a corresponding site on the other side of the neck.

Reading of the skin reactions after tuberculin injection:
The injection sites should be palpated carefully to detect reactions 72 hours (+/- 4 hours) after intradermal injection and the skin-fold thickness of each injection site re-measured. The same person should measure the skin before the injection and when the test is read.
Measurements of the injection site must be taken carefully by placing the callipers, where a response (swelling) has been detected, across the broadest width of the swelling, without applying undue pressure.
Clinical signs compatible with bovine tuberculosis must be recorded at the time of reading to assist in the identification of animals that may be exposed but which have not been identified as reactors in the SICCT test (i.e. false negatives).

The presence of clinical signs 72 hours after injection of tuberculin PPD, such as diffuse or extensive oedema, exudation, necrosis, pain or inflammation of the lymphatic ducts in that region or of the regional (pre-scapular) lymph nodes, is indicative of likely exposure to *Mycobacterium* species causing bovine tuberculosis (i.e., a member of the *Mycobacterium tuberculosis* complex). The person performing the test should carefully examine and record any such signs. Especially in case of necrosis in absence of any other clinical signs that are symptomatic of bovine tuberculosis, the tester should be cautious in making the correct interpretation. In case of doubt the competent authority may require additional diagnostic measures.

Interpretation of the SICCT test results:
For the establishment and maintenance of officially tuberculosis-free herd status for the purpose of internal EU trading in bovines, the interpretation of the skin reactions induced by the bovine and avian tuberculin PPD injections should be made according to the guidelines ("Intradermal Tuberculin Skin Test Protocol in Bovine Animals") published by the EU Reference Laboratory for bovine tuberculosis at: https://www.visavet.es/bovinetuberculosis/databases/protocols.php

Interpretation of skin reactions of the SICCT test	**Clinical observations and the recorded increases in skin-fold thickness at the sites of injection 72 hours after injection of the Tuberculin PPDs.**
Reactor	A reaction to bovine tuberculin PPD which is more than 4 mm greater than the reaction to avian tuberculin PPD, or the presence of clinical signs.
Inconclusive reactor	A reaction to bovine tuberculin PPD (of at least 2 mm) which is from 1 to 4 mm greater than the reaction to avian tuberculin PPD, and the absence of clinical signs.
Negative	A reaction to bovine tuberculin PPD which is equal to or less than the reaction to avian tuberculin PPD, and the absence of clinical signs.

Animals with an inconclusive SICCT test result that are not immediately removed, either voluntarily by the animal owner or by the competent authority, shall be subjected to another test after a minimum of 42 days. Animals, that are not negative to this second test, shall be deemed positive to the test (reactors).

The national competent authority may require a more severe interpretation of the skin reactions to bovine and avian tuberculin PPDs.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

The reactions seen after administration of an overdose are the same as those described under 3.6.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

For administration only by a veterinarian. The import, sale, supply and/or use of Tuberculin PPD Kit is restricted or prohibited in Ireland pursuant to national animal health policy. Any person intending to import, sell supply and/or use Tuberculin PPD Kit must consult the Department of Agriculture on the current vaccination policies prior to import, sale, supply and/or use.

3.12 Withdrawal periods

Zero days.

4. IMMUNOLOGICAL INFORMATION

4.1 ATCvet code :

Bovine Tuberculin PPD 3000: QI02AR01
Avian Tuberculin PPD 2500: QI02AR02

These products are *in vivo* diagnostic substances to diagnose the state of immunity of cattle against bovine tuberculosis.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Do not mix with any other veterinary medicinal product.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale:
The veterinary medicinal product comprises two components with the following shelf-lives:

Bovine Tuberculin PPD 3000:
- 20-dose presentation: 4 years
- 50-dose presentation: 4 years

Avian Tuberculin PPD 2500:
- 20-dose presentation: 4 years
- 50-dose presentation: 4 years

The shelf-life of the veterinary medicinal product is specified as the shelf-life of the component with the earliest expiry date.

Shelf life after first opening the immediate packaging:
Use immediately.

5.3 Special precautions for storage

Store in a refrigerator (2 °C - 8 °C).
Do not freeze.
Keep the vials in the polystyrene box, closed with carton sleeve, in order to protect from light.

Transportation:
May be transported at 2 °C - 37 °C for a period not longer than 14 days.
Do not freeze.
Keep the vials in the polystyrene box, closed with carton sleeve, in order to protect from light.

5.4 Nature and composition of immediate packaging

<u>The 20-dose presentation of the veterinary medicinal product:</u>
Polystyrene box with 20 vials (hydrolytic Type I) of Bovine Tuberculin PPD 3000 and 20 vials (hydrolytic Type I) of Avian Tuberculin PPD 2500. Each vial contains 20 doses of 0.1 ml.

<u>The 50-dose presentation of the veterinary medicinal product:</u>
Polystyrene box with 10 vials (hydrolytic Type I) of Bovine Tuberculin PPD 3000 and 10 vials (hydrolytic Type I) of Avian Tuberculin PPD 2500. Each vial contains 50 doses of 0.1 ml.

The vials are closed with a rubber-butyl stopper and sealed with an aluminium cap (blank cap for Bovine Tuberculin PPD 3000 and red cap for Avian Tuberculin PPD 2500). The box is closed with a labelled carton sleeve. A package leaflet is included.

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Prionics Lelystad B.V.

7. MARKETING AUTHORISATION NUMBER(S)

VPA10526/001/001

8. DATE OF FIRST AUTHORISATION

26/11/2010

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

17/04/2026

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).