

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE IMMUNOLOGICAL VETERINARY MEDICINAL PRODUCT

Tuberculin PPD Kit

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Bovine Tuberculin PPD 3000:

Per 0.1 ml (1 dose):

Active substance:

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

Other excipients:

Phenol: 0.4 – 0.5 mg

For the full list of excipients, see section 6.1

Avian Tuberculin PPD 2500:

Per 0.1 ml (1 dose):

Active substance:

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

Other excipients:

Phenol: 0.4 – 0.5 mg

Ponceau 4R (E 124): 5 microgram

For the full list of excipients, see Section 6.1

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

3. PHARMACEUTICAL FORM

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.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle.

4.2 Indications for use, specifying the 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 and comparing the degree of skin swelling of the two injection sites enables differentiation between the specific reaction in target species exposed to *Mycobacterium* species causing bovine tuberculosis and the non-specific reaction in target species, which have been exposed to other species of *Mycobacteria* or related genera, causing cross sensitisation to Bovine Tuberculin PPD 3000.

4.3 Contra-indications

None.

4.4 Special warnings

For a reliable result of the Single Intradermal Comparative Cervical Tuberculin (SICCT) test the use of the Tuberculin PPD Kit in cattle should be avoided within 42 days following a previous administration of tuberculin PPDs. In specific circumstances, a time interval shorter than 42 days may not be avoided e.g. when a herd undergoing test may include recently acquired (and tested) animals. However, it has been observed that a shorter time interval between tests results in a potential loss of skin responsiveness and is therefore not recommended.

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

The reliability of the test is also influenced by the site of injection of the tuberculin PPD (see 4.9) and by the amount of tuberculin PPD administered; doses less than the prescribed amount of 0.1 ml are likely to lead to a false result of the SICCT test.

The sensitivity of the test can be influenced by concurrent infection with *Mycobacterium* species 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, might also contribute to a lower sensitivity. Notice must be taken that the response is ordinarily somewhat depressed in the peri-parturient period. In the event of a fulminating infection a response to the intradermal test can even be absent.

4.5 Special precautions for use, including special precautions to be taken by the person administering the immunological veterinary medicinal product

Special precautions for use in animals

Not applicable.

Special precautions to be taken by the person administering the immunological 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 expect a 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. If a strong reaction or systemic symptoms occur seek medical advice immediately. Show the package leaflet or the label to the physician.

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.

4.6 Adverse reactions

A swelling of the skin is very common at the injection sites shortly after the 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, unless the animal has become sensitised to other species of Mycobacteria capable of causing a non-specific reaction. In infected cattle and/or in cattle sensitised with non-specific mycobacteria the initial swelling, in uncommon cases up to 65 mm, will also decrease in size within 24 hours but it will take up to 4 weeks before the swelling has completely disappeared. In infected cattle a small rise in body temperature, which will return to normal within 24 hours, can occur but is uncommon.

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 Bovine and/or Avian Tuberculin PPD does not have a negative effect on reproductive performance or lactation.

4.8 Interaction with other veterinary 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 due to the administration of tuberculin PPDs.

Where administration of a medicinal product is necessary such product should not be administered near to the injection sites of the Tuberculin PPD Kit and preferably not on the same side of the neck.

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

In particular, the Tuberculin PPD Kit 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.

4.9 Amounts to be administered and administration route

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 is about four inches (10 cm) below the crest. The lower site 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, which have non-associated lumps or swellings proximal to 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 any abnormalities near to the injection site(s) should be recorded. The presence of skin tuberculosis should also be recorded.

Measurement of skin thickness prior 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 tuberculin test after 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 Single Intradermal Comparative Cervical Tuberculin (SICCT) test:

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 following instructions (as described in section 2.2.5.3.2 of Annex B of Council Directive 64/432/EEC).

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.
Positive reaction	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 reaction	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 reaction	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 inconclusive to the SICCT test that are not 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, which are not negative to this second test, shall be deemed positive to the test.

National requirements for a more severe interpretation of the skin reactions may apply.

4.10 Overdose (signs, emergency procedure, antidotes), if necessary

The reactions seen after administration of an overdose are the same as those described under 4.6.

4.11 Withdrawal periods

Zero days.

5. IMMUNOLOGICAL PROPERTIES

ATCvet code(s):

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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenol

Glucose anhydrous

Disodium phosphate dihydrate

Potassium dihydrogen phosphate

Water for injections

Ponceau 4R (E124)*

* The colouring agent Ponceau 4R (E 124) is only present in Avian Tuberculin PPD 2500.

6.2 Incompatibilities

Do not mix with any other veterinary medicinal product.

6.3 Shelf-life

Shelf-life of the immunological veterinary medicinal product as packed for sale:

The Tuberculin PPD Kit comprises two components with the following shelf-lives:

Bovine Tuberculin PPD 3000:

- 20-doses presentation: 4 years
- 50-doses presentation: 4 years

Avian Tuberculin PPD 2500:

- 20-doses presentation: 4 years
- 50-doses presentation: 4 years

The shelf-life of the Tuberculin PPD Kit is specified as the shelf-life of the component with the earliest expiry date.

Shelf-life after first opening the immediate packaging:

Use immediately.

6.4 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.

6.5 Nature and composition of immediate packaging

The 20-doses presentation of the Tuberculin PPD Kit:

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.

The 50-doses presentation of the Tuberculin PPD Kit:

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.

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

Any unused product or waste material derived from such products should be disposed of in accordance with national requirements.

7. MARKETING AUTHORISATION HOLDER

Prionics Lelystad BV
Platinastraat 33
8211 AR Lelystad
The Netherlands

8. MARKETING AUTHORISATION NUMBER

Vm 36410/4000

9. DATE OF THE FIRST AUTHORISATION

24 November 2010

10. DATE OF REVISION OF THE TEXT

December 2018

PROHIBITION OF SALE, SUPPLY AND/OR USE

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

Approved: 18 April 2019

