

B. PACKAGE LEAFLET

Tuberculin PPD Kit

(Bovine Tuberculin PPD 3000 and Avian Tuberculin PPD 2500)

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PACKAGE LEAFLET

Tuberculin PPD Kit

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

Prionics Lelystad B.V.
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2. NAME OF THE IMMUNOLOGICAL VETERINARY MEDICINAL PRODUCT

Tuberculin PPD Kit
Solution for injection

The Tuberculin PPD Kit is composed of Bovine Tuberculin PPD 3000 and Avian Tuberculin PPD 2500.

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

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 ingredients:

Phenol:
mg

0.4 – 0.5

Glucose, anhydrous
Disodium phosphate dihydrate
Potassium dihydrogen phosphate
Water for injections

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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 ingredients:

Phenol:	0.4 – 0.5
mg	
Ponceau 4R (E 124):	5
microgram	
Glucose, anhydrous	
Disodium phosphate dihydrate	
Potassium dihydrogen phosphate	
Water for injections	

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

4. INDICATION(S)

To be used for the *in vivo* identification of cattle which have been exposed to *Mycobacterium* species causing bovine tuberculosis.

5 CONTRA-INDICATIONS

None.

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 or 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)

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- very rare (less than 1 animal in 10,000 animals, including isolated reports)

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

7 TARGET SPECIES

Cattle.

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

Dosage:

0.1 ml of Bovine Tuberculin PPD 3000 and 0.1 ml of Avian Tuberculin PPD 2500.

Route of administration:

Intradermal injection.

Method of administration:

See for details section 9 "Advice on correct administration".

Use appropriate Tuberculin testing equipment like the "McLintock" pre-set syringe.

9. ADVICE ON CORRECT ADMINISTRATION

The Tuberculin PPD Kit is used to perform the Single Intradermal Comparative Cervical Tuberculin (SICCT) test.

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 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:

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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.

The needle should be introduced, bevel edge outwards and graduated syringe charged with tuberculin PPD attached, into the skin in such a manner as to ensure the intradermal delivery of the tuberculin PPD. This usually requires the insertion of the needle at a narrow angle to the skin. The insertion of the needle at a right angle to the skin will generally result in a subcutaneous injection being made. Such injections give rise to false negative results and must be avoided. Considerable pressure on the plunger of the syringe is usually necessary to make an intradermal injection. Absence of resistance to the flow of the tuberculin is an indication that it has not been injected intradermally, or that the syringe is leaking or improperly loaded. The dose (0.1 ml) of tuberculin PPD solution is then injected.

A correct injection is confirmed by palpating a small pea-like swelling at each site of injection. 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

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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.

10. WITHDRAWAL PERIOD

Zero days.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of reach and sight of children

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.

Do not use after the expiry date which is stated on the vial label and carton box label.

Should be used immediately after first opening.

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12 SPECIAL WARNING(S)

Concomitant administration of other products:

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.

Animals treated with immunosuppressive medicinal products

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.

Mixing with other veterinary medicinal products:

Do not mix with any other veterinary medicinal product.

Animals vaccinated against John's Disease:

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.

Reliability and sensitivity of the SICCT test:

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.

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The reliability of the test is also influenced by the site of injection of the tuberculin PPD 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.

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.

Accidental self-injection:

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.

Overdose:

The reactions seen after administration of an overdose are the same as those described under section 6 "Adverse reactions".

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.

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

It is essential that the remainder of all test materials employed in the test procedure, including disposable syringe parts, used and broached tuberculin vials, cartons and other items are gathered and removed at the time of leaving the holding. Used and broached vials should be stored in a designated receptacle and returned to the administrative centre regularly for safe and proper disposal in accordance with national requirements. The safe and proper disposal of used materials is the responsibility of the person conducting the test.

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14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

TBD

15. OTHER INFORMATION

The 20-doses presentation of the Tuberculin PPD Kit:
Polystyrene box with 20 vials of Bovine Tuberculin PPD 3000 and 20 vials 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 of Bovine Tuberculin PPD 3000 and 10 vials of Avian Tuberculin PPD 2500. Each vial contains 50 doses of 0.1 ml.

The vials are closed with a rubber 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.

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

In case of an adverse event you should contact the marketing authorisation holder (see section 1).

For animal treatment only.

UK only
Vm 36410/4000

POM-V

To be supplied only on veterinary prescription

IE only
VPA 10526/001/001

VPO-1

Veterinary Practitioner Only
For administration only by a veterinary practitioner

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AN:

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Approved: 18 April 2019

A handwritten signature in black ink, appearing to read "Omuobb", with a horizontal line underneath the name.