TUBERCULIN PPD RT 23 AJV
FOR MANTOUX TESTING

Solution for injection

1 Composition

Active ingredient
One single dose of 2 T.U./0.1 mL contains 0.04 microgram of Tuberculin PPD RT 23.

Excipients
Disodium phosphate dihydrate, potassium dihydrogen phosphate, sodium chloride, potassium hydroxyquinoline sulphate, polysorbate 80 and water for injections.

2 Clinical particulars

2.1 Therapeutic indications
Tuberculin PPD RT 23 AJV is used for Mantoux tuberculin skin testing to diagnose if an individual has ever been infected with *Mycobacterium tuberculosis*. Some countries also recommend Mantoux tuberculin skin testing in conjunction with BCG vaccination, either to ensure that only tuberculin-negative individuals are vaccinated or as a post-vaccination test.
Tuberculin PPD RT 23 AJV can be used in all age groups.

This medicinal product is for diagnostic use only.

2.2 Dosage and administration
Dosage and strength
The dosage is always 0.1 mL regardless of the strength used.
Tuberculin PPD RT 23 AJV is injected intradermally.
The strength 2 T.U./0.1 mL is recommended.

Injection technique
- 0.1 mL is administered with a 1 mL graduated syringe fitted with a short bevel needle (gauge 25 or 26).
- The injection must be given strictly intradermally on the flexor surface of the forearm at the junction of the upper third with the lower two-thirds. Administration near the wrist or the elbow joint may weaken the reaction.
- The skin is slightly stretched, and the needle is held almost parallel with the skin surface, with the bevel upwards. The tip of the needle is inserted into the superficial layer of the dermis.
- The needle should be visible through the epidermis during insertion. The 0.1 mL is slowly injected and a small blanched papule of 8–10 mm in diameter appears. This papule will disappear after approximately 10 minutes.
- If no papule appears, the injection has been given too deep, and the skin test should be repeated on the other arm or on the same arm, at least 4 cm away from the first injection site.

National recommendations regarding the administration of the Mantoux tuberculin skin test may be taken into consideration.

Evaluating the reaction
A skin test reaction is seen as a flat, uneven, slightly raised induration surrounded by an area of redness.
The induration should be evaluated 48–72 hours after the injection. After approximately 72 hours, the size of the induration is expected to diminish. Only the induration is assessed.
The diameter of the induration is measured in millimetres transversely to the long axis of the forearm with a transparent, flexible plastic ruler.
Recommendations for interpreting the Mantoux tuberculin skin test are shown in Table 1.

Diameter of induration in millimetres		
Negative 0–5 mm	Positive 6–14 mm	Strongly positive +15 mm

Table 1: Normal interpretation of the skin test result.

Alternative interpretations, depending on national recommendations, individual and epidemiological factors, may be applied.

Interpretation
A positive reaction indicates an immune response for one or more of the following reasons:
- Infection with *Mycobacterium tuberculosis* complex, including *M*. *tuberculosis*, *M*. *bovi*s, *M*. *africanum*, *M*. *microtii* or *M*. *tuberculosis* subsp.*caprae*.
- Infection with non-tuberculous mycobacteria.
- Previous BCG vaccination. BCG-vaccinated individuals normally become tuberculin-positive after 4–8 weeks.

Reactions larger than 15 mm are unlikely to be due to previous BCG vaccination or exposure to environmental mycobacteria.

Waning of tuberculin sensitivity
In most individuals, tuberculin sensitivity caused by infection with *M*. *tuberculosis* or related mycobacteria normally persists throughout life, but may decrease or disappear gradually in some individuals.
The tuberculin sensitivity frequently wanes within a few years in BCG-vaccinated individuals.

Booster effect
If tuberculin is administered to individuals whose tuberculin sensitivity has waned, the reaction to the skin test will be weak or absent.
Retesting with tuberculin weeks or months later may result in an accentuation of the response, i.e. a booster effect.

Repeated tuberculin skin testing will not induce a positive reaction in individuals who have no previous cellular immunity against the antigens in tuberculin PPD.

Repeated tuberculin skin testing
If the tuberculin skin test is likely to be repeated, e.g. in health care workers potentially exposed to tuberculosis infection, a two-step method is recommended. Individuals with a weak or an absent initial Mantoux tuberculin skin test should undergo a second tuberculin skin test 2–4 weeks after the first test.
Skin test conversion in such individuals is defined as a reaction to the second test of more than 10 mm and an increase of at least 6 mm compared to the first test.
Individuals with skin test conversion after the second test should be considered to be previously infected with mycobacteria or may have been BCG vaccinated, whereas those with a negative reaction to the second test should be considered uninfected.

It is important to emphasise that the predictive value of the skin test result and the expected risk of tuberculosis should be considered on an individual basis.

2.3 Contraindications
Tuberculin PPD RT 23 AJV should not be administered to:
- Individuals known to be hypersensitive (Type I) to the active substance or any of the excipients of the medicinal product listed in section 1.
- Individuals who previously have experienced a severe local reaction to tuberculin products. A severe local reaction may include vesicles and ulceration at the injection site and skin necrosis at the centre of a widespread tuberculin reaction. The necrosis will generally disappear after a few days.

2.4 Special warnings and precautions for use
Although anaphylaxis is rare, facilities for its management should always be available during the Mantoux tuberculin skin test.
Whenever possible skin tested individuals should be observed for allergic reactions for up to 20 minutes after administration.

Avoid subcutaneous or intramuscular injection of Tuberculin PPD RT 23 AJV. If this occurs, a papule will not develop and the Mantoux tuberculin skin test should be repeated on the other arm or on the same arm, at least 4 cm away from the first injection site.

2.5 Interaction with other medicinal products and other forms of interaction
A variety of host-related factors such as age, nutrition, renal failure, diabetes, immunosuppression by medicinal products (e.g. corticosteroids) or disease, e.g. cancer, HIV infection or sarcoidosis can cause

false-negative tuberculin reactions. Viral infections (particularly measles, mumps, mononucleosis, varicella and influenza) can lower the tuberculin reactivity for a few months.

Reduced tuberculin reactivity may be observed after vaccinations with live virus (e.g. vaccines against measles, mumps and rubella). This decreased tuberculin reactivity may result in false-negative reactions. Therefore, if Mantoux tuberculin skin testing cannot be done at the same time as measles, mumps and rubella immunisation, the test should be postponed for 4–6 weeks.

Tuberculin PPD RT 23 AJV can be safely administered simultaneously with all live and inactivated vaccines.

Many patients co-infected with HIV and *M*. *tuberculosis* have anergy for tuberculin. In patients with severe tuberculosis (e.g. miliary tuberculosis) tuberculin reactivity may be suppressed.

Previous BCG vaccination or recent infection with environmental non-tuberculous mycobacteria can result in cross-sensitisation and a false-positive reaction to a Mantoux tuberculin skin test.

2.6 Pregnancy and lactation
Although Mantoux tuberculin skin testing with Tuberculin PPD RT 23 AJV is considered safe during pregnancy and lactation, there have been no controlled studies on pregnant women. It should therefore be used on a pregnant woman only if clearly needed.

2.7 Effects on ability to drive and use machines
Tuberculin PPD RT 23 AJV has no or negligible influence on the ability to drive and use machines.

2.8 Undesirable effects
The most common adverse reactions after administration of Tuberculin PPD RT 23 AJV are pain, itching and irritation at the injection site.

Common (≥ 1/100 to < 1/10)	Injection site pain Injection site itching Injection site irritation
Uncommon (≥ 1/1,000 to < 1/100)	Lymphadenopathy Fever
Rare (≥ 1/10,000 to < 1/1,000)	Skin necrosis Injection site vesiculation
Very rare (< 1/10,000)	Hypersensitivity, including anaphylactic reactions
Frequency not known	Headache Urticaria Injection site ulceration

2.9 Overdose
Based on accumulated evidence from spontaneous reports, the effect of an overdose is not significantly different from those described under undesirable effects.

3 Pharmaceutical particulars

3.1 Incompatibilities
This medicinal product must not be mixed with other medicinal products.

3.2 Storage conditions
Store at 2–8°C in the original package in order to protect from light. Use within 24 hours after first opening of the vial. Store at 2–8°C in the original package after opening.

4 Manufacturer

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