# PROFESSIONAL INFORMATION

## SCHEDULING STATUS

**S2**

## 1 NAME OF THE MEDICINE

**Tuberculin PPD RT/23 2 TU / 0,1 ml** solution for injection

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One single dose of Tuberculin PPD RT/23 2 TU / 0,1 ml contains 0,04 micrograms of Tuberculin PPD RT/23.

*Preservative:*

Potassium hydroxyquinoline sulphate 0,01 % *m/v*

Sugar free.

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Solution for injection.

A clear, colourless to pale-yellow solution without particles.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Tuberculin PPD RT/23 2 TU / 0,1 ml is used for Mantoux tuberculin skin testing to diagnose if an individual has ever been infected with *Mycobacterium tuberculosis*.

### 4.2 Posology and method of administration

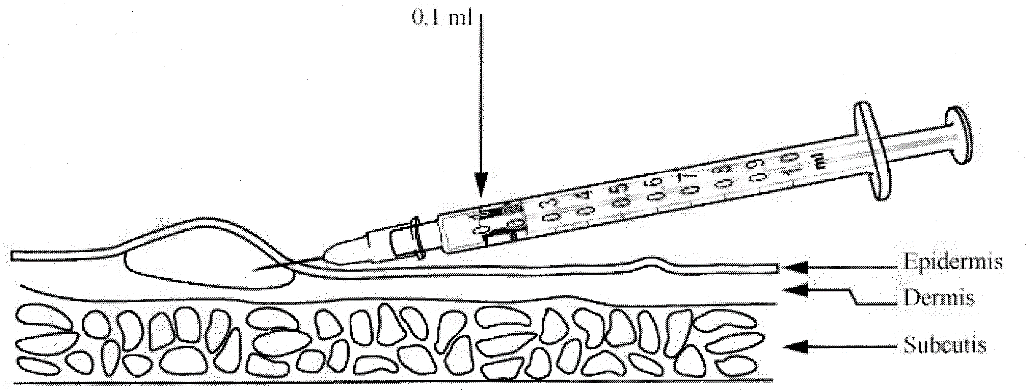
**Posology**

The dosage is 0,1 ml.

Tuberculin PPD RT23 2 TU / 0,1 ml is injected intradermally.

**Method of administration**

- 0,1 ml Tuberculin PPD RT/23 2 TU / 0,1 ml must be administered with a 1 ml graduated syringe fitted with a 25 or 26 gauge, short bevel needle.
- The injection must be given intradermally in the middle third of the forearm. Administration near the wrist or the elbow joint may weaken the reaction.
- The skin is slightly stretched and the needle point 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 must be visible through the epidermis during insertion. 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 (see section 4.4).




**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. 1 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.

**Table 1: Normal interpretation of the skin test result.**

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

**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. bovis*, *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.

The interpretation of the Mantoux tuberculin skin test can be influenced by factors mentioned under section 4.5. In countries where BCG vaccination is widely used and where Tuberculin PPD RT/23 2 TU / 0,1 ml is used as a post-vaccination test, it may be necessary to use an alternative interpretation with a larger diameter of the induration as a positive reaction.

An induration measured to be close to the limit should be interpreted with caution and the results should be related to the clinical situation.

Special caution should be taken in the interpretation of results measured to be close to the limit in individuals who are in close contact with patients with infectious TB, in the TB screening of

immunosuppressed individuals including HIV infected children and adults, suspected TB infected infants; patients treated with immunosuppressants such as TNF-alpha inhibitors and in individuals with other risk factors such as children and adolescents, pregnant women, patients with diabetes mellitus or with other predisposing conditions.

**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 RT/23 2 TU / 0,1 ml.

**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.

### 4.3 Contraindications

- Hypersensitivity (Type I) to Tuberculin PPD RT23 or to any of the excipients of Tuberculin PPD RT23 2 TU / 0,1 ml (see section 6.1)
- Individuals who 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.
- Individuals who have previously been diagnosed with tuberculosis or any other mycobacterial disease.

### 4.4 Special warnings and precautions for use

Exaggerated reactions may occur when used in persons with active tuberculosis.

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 RT23 2 TU / 0,1 ml. 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.

Tuberculin PPD RT23 2 TU / 0,1 ml contains less than 1 mmol potassium (39 mg) and less than 1 mmol sodium (23 mg) per dose, i.e. essentially potassium- and sodium-free.

## 4.5 Interaction with other medicines and other forms of interaction

A variety of host-related factors such as age, nutrition, renal failure, diabetes, immunosuppression by medicines (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.

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.

After vaccinations with vaccines containing live virus, e.g. vaccines against measles, mumps and rubella, a reduced reactivity may be observed. This decreased 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 RT23 2 TU/0,1 ml 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.

## 4.6 Fertility, pregnancy and lactation

**Pregnancy**

Tuberculin PPD RT23 2 TU / 0,1 ml can be used during pregnancy.

**Breastfeeding**

Tuberculin PPD RT23 2 TU / 0,1 ml can be used during breastfeeding.

**Fertility**

No clinical or non-clinical data are available on the possible effects of Tuberculin PPD RT23 2 TU / 0,1 ml on male and female fertility.

## 4.7 Effects on ability to drive and use machines

Tuberculin PPD RT23 2 TU / 0,1 ml has no or negligible influence on the ability to drive and use machines.

## 4.8 Undesirable effects

**a. Summary of the safety profile**

The adverse events following administration of Tuberculin PPD RT23 2 TU/0,1 ml are generally mild and transient.

The most common adverse reactions after administration of Tuberculin PPD RT23 2 TU/0,1 ml are pain, itching and irritation at the injection site. Individuals very sensitive to tuberculin may experience vesicles and necrosis at the injection site. The necrosis will usually disappear after a few days. Mild fever and enlargement of the lymph nodes may occur.
There is an extensive clinical experience with Tuberculin PPD RT23 2 TU/0,1 ml and the safety profile is well known.

**b. Tabulated summary of adverse reactions**

The following convention was used for frequency grouping: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1 000 to <1/100); rare (≥1/10 000 to <1/1 000); very rare (<1/10 000); not known (cannot be estimated from the available data).

| **MedDRA system organ class** | **Frequency** | **Adverse reactions** |
|---|---|---|
| Blood and lymphatic system disorders | Uncommon | Lymphadenopathy |
| Immune system disorders | Very rare | Hypersensitivity, including anaphylactic reactions |
| Nervous system disorders | Not known | Headache |
| Skin and subcutaneous tissue disorders | Rare | Skin necrosis |
| | Not known | Urticaria |
| General disorders and administration site conditions | Common | Injection site pain, injection site itching, injection site irritation |
| | Uncommon | Fever |
| | Rare | Vesicles at the injection site |
| | Not known | Injection site ulceration |

*Reporting of suspected adverse reactions*

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions & Quality Problem Reporting Form**", found online under SAHPRA's publications: https://sahpra.org.za/wp-content/uploads/2020/01/6.04_ARF1_v5.1_27Jan2020.pdf

## 4.9 Overdose

See section 4.8. Treatment is symptomatic and supportive, but undesirable effects in relation to overdosage are not expected.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

A.30.2 Biologicals antigens

Pharmacotherapeutic group: Diagnostic agents, tuberculosis diagnostics, ATC code: V04CF01

Tuberculin PPD RT/23 2 TU / 0,1 ml is a tuberculosis diagnostics agent.

The active substances are the proteins, lipids and polysaccharides and other bacterial fragments obtained in the culture filtrate of tubercle bacilli from which the tuberculin was originally prepared, which cause induration as a specific skin 25 response of the delayed type at the site of injection in individuals infected with tuberculosis. Induration may be palpable as early as 5 hours after injection, but normally reaches a peak only after 48 to 72 hours. The reaction subsides over the course of several days.

### 5.2 Pharmacokinetic properties

Not applicable for Tuberculin PPD RT23 2 TU/0,1 ml as it is an immunological medicine.

### 5.3 Preclinical safety data

No formal preclinical or toxicological studies have been performed on Tuberculin PPD RT23 2 TU/0,1 ml.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Disodium phosphate dihydrate

Polysorbate 80

Potassium dihydrogen phosphate

Potassium hydroxyquinoline sulphate

Sodium chloride

Water for injections

## 6.2 Incompatibilities

Tuberculin PPD RT/23 2 TU/0,1 ml must not be mixed with other medicines.

## 6.3 Shelf life

36 months.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and should not be longer than 24 hours at 2°C – 8°C.

## 6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).

Do not freeze.

Store in the original package in order to protect from light.

For storage condition after first opening of the medicine, see section 6.3.

## 6.5 Nature and contents of container

Tuberculin PPD RT/23 2 TU / 0,1 ml is packed as 1,5 ml solution in multi-dose glass vial (type I) closed with a stopper (chlorobutyl rubber) in pack sizes of 1 or 10.

Not all pack sizes may be marketed.

## 6.6 Special precautions for disposal and other handling

Any remaining liquid should be discarded. It is recommended that the vials with unused content and the needles/syringes used to administer the liquid should be disposed in a waste container for hospital waste.

Tuberculin PPD RT23 SSI 2 TU / 0,1 ml does not contain any live material.

## 7 HOLDER OF CERTIFICATE OF REGISTRATION

Kahma Biotech (Pty) Ltd.

106, 16th Road

Midrand, 1686

Gauteng

South Africa

## 8 REGISTRATION NUMBERS

28/30.2/0356

| |
|---|
| Botswana: S2<br>Reg No.: BOT0600874 |

| |
|---|
| Namibia: NS2<br>Reg No.: 04/30.1/1430 |

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 29 December 1993

## 10 DATE OF REVISION OF THE TEXT

20 September 2023