Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Tuberculin PPD RT23 AJV 2 T.U./0.1 mL, solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Tuberculin PPD RT 23.

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

Excipients with known effect

Disodium phosphate dehydrate	0.76 mg
Potassium dihydrogen phosphate	0.145 mg
Sodium chloride	0.48 mg
Potassium hydroxyquinoline sulphate	10 µg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless to pale-yellow solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Tuberculin PPD RT23 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 RT23 AJV is indicated for all age groups.

This medicinal product is for diagnostic use only.

4.2 Posology and method of administration

Posology

The dosage is 0.1 mL.
Tuberculin PPD RT23 AJV is injected intradermally.

Method of administration

In the following a detailed description of administration of Tuberculin PPD RT23 AJV is given:

- 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 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 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 (see section 4.4).

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 and should decrease after this. 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	Positive	Strongly positive
0–5 mm	6–14 mm	+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. 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.

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.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

Tuberculin PPD RT23 AJV should not be administered to:

- 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.

4.4 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 RT23 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.

This medicine 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'.

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

4.5 Interaction with other medicinal products and other forms of interactions

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 reactivity may be observed after vaccinations with live virus (e.g. vaccines against measles, mumps and rubella). 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 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.

4.6 Fertility, pregnancy and lactation

Animal reproduction studies have not been performed with Tuberculin PPD RT23 AJV.

Women of childbearing potential
Tuberculin PPD RT23 AJV is considered safe.

Contraception in males and females
Tuberculin PPD RT23 AJV is considered safe.

Pregnancy
Tuberculin PPD RT23 AJV can be used during pregnancy.

Breastfeeding
Tuberculin PPD RT23 AJV can be used during breast-feeding.

Fertility
No clinical or non-clinical data are available on the possible effects of Tuberculin PPD RT23 AJV on male and female fertility.

4.7 Effects on ability to drive and use machines

Tuberculin PPD RT23 AJV has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile
The adverse events following administration of Tuberculin PPD RT23 AJV are generally mild and transient.

The most common adverse reactions after administration of Tuberculin PPD RT23 AJV are pain, itching and irritation at the injection site. Individuals very sensitive to tuberculin may experience vesiculation, ulceration 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.

Tabulated list of adverse reactions
There is an extensive clinical experience with Tuberculin PPD RT23 AJV and the safety profile is well known.

Blood and lymphatic system disorders Uncommon (≥ 1/1,000 to < 1/100)	Lymphadenopathy
Immune system disorders Very rare (< 1/10,000)	Hypersensitivity, including anaphylactic reactions
Nervous system disorders Not known (cannot be estimated from the available data)	Headache
Skin and subcutaneous tissue disorders Rare (≥ 1/10,000 to < 1/1,000) Not known (cannot be estimated from the available data)	Skin necrosis Urticaria
General disorders and administration site conditions Common (≥ 1/100 to < 1/10) Uncommon (≥ 1/1,000 to < 1/100) Rare (≥ 1/10,000 to < 1/1,000) Not known (cannot be estimated from the available data)	 Injection site pain Injection site itching Injection site irritation Fever Injection site vesicles Injection site ulceration

Description of selected adverse reactions

Anaphylactic shock

For precautions regarding anaphylactic shock please see section 4.4.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

Undesirable effects in relation to overdosage are not expected.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic agents, tuberculosis diagnostics, ATC code: V04CF1
Therapeutic subgroup: V04 diagnostic agents
Pharmacological subgroup: V04C other diagnostic agents
Chemical subgroup: V04CF Tuberculosis diagnostics

5.2 Pharmacokinetic properties

Not applicable for Tuberculin PPD RT23 AJV as an immunological medicinal product.

5.3 Preclinical safety data

No formal preclinical or toxicological studies have been performed on Tuberculin PPD RT23 AJV.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium phosphate dihydrate
Potassium dihydrogen phosphate
Sodium chloride
Potassium hydroxyquinoline sulphate
Polysorbate 80
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

3 years.

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 (2ºC – 8ºC).

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

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

1.5 mL solution in multi-dose glass vial (type I) closed with a stopper (chlorobutyl rubber) in pack sizes of 1 or 10. The stoppers do not contain latex.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

AJ Vaccines A/S
Artillerivej 5
DK-2300 Copenhagen S
Denmark

8 MARKETING AUTHORISATION NUMBER

PA2160/004/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23 April 1997

Date of last renewal: 23 April 2007

10 DATE OF REVISION OF THE TEXT

January 2022