Tuberculine PPD-T®

Tuberculine purified protein derivative for human use (intradermal Mantoux test)

Solution for injection

One dose (0.1 mL) contains:
- Tuberculine purified protein derivative for human use 3 IU
  - with box with 10 vials of 2.5 mL

Read all of this leaflet carefully before you start using this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others.
  It can harm them, even if they have the same signs of illness as you do.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Tuberculine PPD-T® is and what it is used for
2. Before you use Tuberculine PPD-T®
3. How to use Tuberculine PPD-T®
4. Possible side effects
5. How to store Tuberculine PPD-T®
6. Further information

1. WHAT TUBERCULIN PPD-T® IS AND WHAT IT IS USED FOR

Tuberculine PPD-T® is a solution obtained by purification of Mycobacterium tuberculosis liquid culture filtrate, which is applied intradermally (Mantoux test). It belongs to the pharmacotherapeutic group of diagnostic devices. Intradermally injected Tuberculine PPD-T® causes a delayed hypersensitivity reaction in persons previously sensitised with Mycobacterium tuberculosis infection. After mycobacterial infection, T cells are sensitised primarily in the regional lymph nodes, thus activating cellular immune response. Proliferation of specific T cells occurs as a response to the infection. After several weeks, these T lymphocytes enter the systemic circulation where they remain for a long period of time. Repeated stimulation of T lymphocytes by intradermally injected tuberculine PPD causes a T cell-mediated local reaction. Tuberculine PPD-T® is used as a diagnostic antigen for detecting hypersensitivity to tuberculin in persons not vaccinated with BCG vaccine, when the need for vaccination is considered. It is applied also as a supplementary diagnostic device in determining Mycobacterium tuberculosis infection in adults suspected of having this infection (including HIV-positive patients) and in children with a high risk of contracting this disease.

2. BEFORE YOU USE Tuberculine PPD-T®

Do not use Tuberculine PPD-T®:
- If you or your child are hypersensitive to the active substance or any other component of this product.
- If you or your child previously manifested a severe skin reaction to this product.

Take special care with Tuberculine PPD-T®

In patients having or suspected to have active tuberculosis, tuberculine test should be carefully applied. Persons with active tuberculosis may manifest more serious and severe local reactions, while in patients with a severe form of tuberculosis (e.g., miliary tuberculosis) tuberculosis reactivity may be suppressed and the test result negative.

Tuberculine reactivity may be reduced (thus causing false negative results) in case of:
- severe bacterial infection and viral infection (HIV infection, infectious mononucleosis, measles, and influenza);
- neoplastic disease (especially lymphoma (malignant disease of lymphocytes, a type of white blood cells)) or UV radiation treatment;
- sarcoidosis (type of inflammatory reaction in which lymphocytes, type of blood cells, react abnormally causing their collection in the affected organs, which results in the disappearance of normal tissue of the affected organ);
- chronic renal insufficiency (weakness);
- dehydration (loss of liquid and electrolytes in the organism) and malnutrition (lack of nutrients in the organism);
- immunosuppression (reduced activity of immune (defense) system) due to illness, surgical interventions or drug administration (administration of 15 mg or more of prednisone per day for minimum one month is considered an immunosuppressive dose of cortico- steroids);
- recent vaccinations with live viral vaccines, such as OPV (oral polio vaccine), MMR vaccine (measles, mumps and rubella vaccine), varicella (chickenpox) or yellow fever vaccine (viral infectious disease) (tuberculine skin test should be postponed for 4-6 weeks after the application of live vaccine, or the test and vaccination should be performed on the same day and the result tests read within 48-72 hours).

According to the World Health Organization recommendation, the use of skin tests and repeated vaccination against tuberculosis are no longer recommended. According to the national immunisation programme, vaccination against tuberculosis is carried out in children immediately after birth, that is, on leaving the maternity hospital or until the second month of life at the latest. If vaccination is not performed in this period, it must be carried out before the first year of life.

Tuberculine PPD-T® is intended for intradermal use only.

It must not be used intravenously, intramuscularly or subcutaneously!

Using other medicines

If you or your child have been recently vaccinated with live viral vaccines, such as OPV (oral polio vaccine), MMR vaccine (measles, mumps and rubella vaccine), varicella (chickenpox) or yellow fever vaccine (viral infectious disease), tuberculine skin test should be postponed for 4-6 weeks after the application of live vaccine, or the test and vaccination should be performed on the same day and the result tests read within 48-72 hours. The preparation must not be mixed with other medicinal products, sera and vaccines in the same syringe.

Using tuberculine PPD-T® with food and drink

Not applicable.

Pregnancy and breastfeeding

Animal reproduction studies have not been performed and no teratogenic effects during tuberculine skin testing in pregnant women have been recorded.

However, contact between a mother having active tuberculosis and her newborn infant immediately after birth entails a high risk of developing tuberculosis in the newborn with serious complications, such as tuberculous meningitis (chronic disease of brain membranes and tissue caused by Koch’s bacillus). Thus, if doctor suspects that a pregnant woman suffers from active tuberculosis, he/she should make a thorough assessment whether the benefits of using this test exceed possible risks and perform the test in the second or third trimester of pregnancy, if necessary.

Driving and using machines

Data not available.

Important information about some of the ingredients of Tuberculine PPD-T®

In case of a known hypersensitivity (allergy) to any of the components of Tuberculine PPD-T®, including excipients (chinoisol, Tween 80), tuberculine test must not be used.

3. HOW TO USE Tuberculine PPD-T®

Posology:

One dose of tuberculine is contained in 0.1 mL of the preparation.

Method of administration:

Tuberculine PPD-T® (Mantoux test) is applied by intradermal injection of one dose (0.1 mL) of the preparation into the front part of the left forearm at the junction of the upper and middle third in the direction of the longer axis.

Tuberculine may be adsorbed on the syringe surface, so the injection should be given without delay.

Disposable tuberculine syringes fitted with appropriate intradermal needles are to be used for tuberculine injection, for each patient individually.

The result is read 48 to 72 hours following the injection, by measuring the diameter of the induration transversely to the longer axis of the forearm. Mantoux test results reading is described in detail at the end of this PIL in the section: Information intended exclusively for medical staff and healthcare workers.

If you use more Tuberculine PPD-T® than you should

Increase in dose reduces the test specificity and increases the risk of side effects.

If you forget to take Tuberculine PPD-T®

Not applicable.

Effects when treatment with Tuberculine PPD-T® is stopped

Not applicable.

4. POSSIBLE SIDE EFFECTS

Tuberculine PPD-T®, as other medicinal products, may cause side effects, although they do not have to manifest in all persons.

Side effects that can occur during the tuberculine test are given as per the following frequency:

- very common > 1/10
- common > 1/100 and < 1/10
- uncommon > 1/1,000 and < 1/100
- rare > 1/10,000 and < 1/1,000
- very rare < 1/10,000

*The estimation of side effects frequency is based on the WHO data.

Although anaphylactic reaction is rare, a proper medical treatment should also always be available following Tuberculine PPD-T® application, in order to react immediately to a potential anaphylactic shock (severe allergic reaction).

Increase in dose reduces the test specificity and increases the risk of side effects.

If any side effect becomes serious, or if you observe any side effect not stated in this leaflet, please inform your doctor or pharmacist about it.

5. HOW TO STORE Tuberculine PPD-T®

Keep Tuberculine PPD-T® out of the reach of children!

Shelf-life

Shelf-life is 6 months.

Do not use Tuberculine PPD-T® after expiry date on the outer packaging. Once the vial is opened for the first time, the preparation should be used within 8 hours, provided that it is stored in a refrigerator at 2°C to 8°C.

Storing

Store the preparation at 2°C to 8°C in a refrigerator, in the original packaging.

Do not freeze.

Empty vials of tuberculine purified protein derivative for human use, vials which are not empty but are not for further use, used syringes, needles and material for disinfection should be disposed of safely in special polyethylene bags and dedicated hard containers and destroyed in accordance with the current regulations.

6. FURTHER INFORMATION

What Tuberculine PPD-T® contains

One dose (0.1 mL of solution) contains:
- Active substance: Tuberculine purified protein derivative for human use
- Excipients:
  - Chinoisol
  - Polysorbate 80
  - Disodium hydrogen phosphate, dihydrate
  - Potassium dihydrogen phosphate
  - Sodium chloride
  - Water for injections
What Tuberculin PPD-T looks like and content of the pack

Tuberculin PPD-T is a colourless to pale-yellow solution, without odour or with a slightly characteristic odour.

Glass vials are of colourless glass type I, volume 3 mL, closed with grey rubber stoppers and alu caps.

Pack size: 10 x 2.5 mL, in a cardboard box.

Marketing Authorisation Holder and Manufacturer

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This leaflet was last approved in January 2012

Dispensing regime:
Tuberculin PPD-T can be administered only in health institutions, under the supervision of an experienced doctor.

Marketing Authorisation number and date:
515 01-4824-11-000 dated 24 February 2012
Marketing Authorisation for Tuberculin PPD-T is conditional and is issued

Information intended exclusively for medical staff and healthcare workers:

Therapeutic indications

Tuberculin PPD-T (intradermal Mantoux test) is used as a diagnostic antigen for detecting hypersensitivity to tuberculosis in persons not vaccinated with BCG vaccine, when the need for vaccination is considered.

Tuberculin PPD-T (intradermal Mantoux test) is applied also as a supplementary diagnostic device in determining Mycobacterium tuberculosi infection in adults suspected of having this infection (including HIV-positive patients) and in children at high risk of contracting this disease.

Posology and method of administration

Tuberculin PPD-T is prepared as a solution for intradermal Mantoux test, which is standardized against the international standard for PPD mammalian so that 0.1 mL of this solution contains 3 IU of tuberculin purified protein derivative. One dose of tuberculin is contained in 0.1 mL of the preparation.

Mantoux test is performed by intradermal injection of one dose (0.1 mL) of the preparation into the front part of the left forearm (at the junction of the upper and middle third) in the direction of the longer axis. Disposable tuberculin syringes fitted with appropriate intradermal needles are to be used for tuberculin injection, for each patient individually. Tuberculin may be adsorbed on the syringe surface, so the injection should be given without delay.

The injection site should be allowed to dry after disinfection. The skin is then slightly stretched and the tip of the needle is inserted into the superficial layer of dermis (the needle is held almost parallel with the skin surface to bevel upwards). The needle should be visible through the epidermis during insertion. The solution is to be slowly injected. The proper injection results in a papule 8-10 mm in diameter which remains for about 10 minutes. If a papule does not appear, the skin test should be repeated on another site. The injection could result in induration surrounded by an area of redness for several hours after injection.

The result is read 48 to 72 hours following the injection, by measuring the diameter of the induration transversely to the longer axis of the forearm. At the site of the tuberculin test application, the induration limits are determined using palpatory method, after which the diameter of the induration is measured in millimetres with a transparent, flexible ruler.

| MANTOUX TEST RESULTS READING (diameter of induration) |
|-----------------|-----------------|-----------------|
| Negative 0-5 mm | Positive 6-14 mm | Strongly positive ≥15 mm |

Negative tuberculin reaction is considered to be the occurrence of induration less than 5 mm in diameter or absence of any change at the injection site.

Persons with a negative reaction, who have not received BCG vaccine, should be vaccinated.

The occurrence of an induration at least 6 mm in diameter with or without red coloring at the injection site is considered as a positive tuberculin reaction. Only the induration is assessed. If necrosis, edema or erythema is present, it is also recorded, but these data are not used in the interpretation of tuberculin test results.

A positive tuberculin reaction indicates an immune response due to the following reasons:

- infection with mycobacteria complex that could cause tuberculosis (M. tuberculosis, M. bovis, M. africanum, M. microti or M. canetti)
- infection with non-tuberculous (atypical) mycobacteria
- previous BCG vaccination (BCG vaccinated persons normally become tuberculin positive after 4-6 weeks)

In following groups of patients, positive values of Mantoux test are closer to the lower limit (within the 6-9 mm range):

- patients with HIV infection or risk factors for this disease in whom the infection has not been determined yet
- persons who have recently been in close contact with the persons suffering from active tuberculosis
- patients having fibrotic changes in lungs (based on the chest x-ray image), as a result of the cured tuberculosis.

Dispensation regime/Place of administration:

Tuberculin PPD-T can be administered only in health institutions, under the supervision of an experienced doctor.

Contraindications

Contraindication for performing tuberculin test is hypersensitivity of the patient to any component of this product.

Tuberculin test must not be used in patients who previously manifested severe skin reaction to this product.

Special warnings and precautions for use

Proper medical treatment must always be at hand so as to react immediately to a possible anaphylactic shock, regardless of the fact that anaphylactic reaction occurs rarely after the tuberculin test (1/1,000).

In patients having or suspected to have active tuberculosis, tuberculin test should be carefully applied. Persons with active tuberculosis may manifest more serious and severe local reactions, while in patients with a severe form of tuberculosis (e.g. miliary tuberculosis), tuberculin reactivity may be suppressed and the reaction be negative.

Tuberculin reactivity may be reduced, thus causing false negative results in certain diseases and conditions or due to the use of certain medications (see the section: Interactions with other medicinal products and other forms of interaction).

Repeated skin testing during a period shorter than one year should be avoided, so that the negative reaction would not become positive. According to the World Health Organization recommendation, the use of skin tests and repeated vaccination against tuberculosis are no longer recommended. According to the national immunization programme, vaccination against tuberculosis is carried out in children younger than 6 years, that is, on leaving the maternity hospital or until the second month of life at the latest. If vaccination is not performed in this period, it must be carried out until the first year of life.

Tuberculin PPD-T is intended for intradermal use only.

It must not be used intravenously, intramuscularly or subcutaneously!

Interactions with other medicinal products and other forms of interaction

Tuberculin reactivity may be reduced (thus causing false negative results) in case of:

- severe bacterial infection and viral infection (HIV infection, infectious mononucleosis, measles, varicella and influenza)
- neoplastic disease (especially lymphoma) or UV radiation treatment
- sarcoidosis
- chronic renal insufficiency
- dehydration and malnutrition
- immunosuppression due to illness, surgical interventions or drug administration (administration of 15 mg or more of prednisone per day for minimum one month is considered an immunosuppressive dose of corticosteroids)
- recent vaccinations with live viral vaccines, such as OPV, MMR vaccine, varicella or yellow fever vaccine (tuberculin skin test should be postponed for 4-6 weeks after the application of live vaccine, or the test and vaccination should be performed on the same day and the test results read within 48-72 hours).

Pregnancy and lactation

Animal reproduction studies have not been performed and no teratogenic effects during tuberculin skin testing in pregnant women have been recorded. However, contact between a mother having active tuberculosis and her newborn infant immediately after birth entails a high risk of developing tuberculosis in the newborn with serious complications, such as tuberculosis meningitis.

Thus, if doctor suspects that a pregnant woman is suffering from active tuberculosis, she/he should make a thorough assessment whether the benefits of using this test exceed possible risks and perform the test in the second or third trimester of pregnancy, if necessary.

Effects on the ability to drive and use machines

Data not available.

Side effects

Tuberculin PPD-T, as other medicinal products, may cause side effects, although they do not have to manifest in all persons.

Side effects that can occur during the tuberculin test are given as per the following frequency:

- very common > 1/10
- common > 1/100, < 1/10
- uncommon > 1/1,000, < 1/100
- rare > 1/10,000, < 1/1,000
- very rare < 1/10,000

* The estimation of side effects frequency is based on the WHO data.

common (>1/100, <1/10)

uncommon (>1/1,000, <1/100)

rare (>1/10,000, <1/1,000)

very rare (<1/10,000)

local pain, irritation or discomfort at the injection site, immediately after administration

systemic: headache, nausea, dizziness, malaise, pyrexia, fever

local: enlargement of regional lymph nodes

systemic: anaphylaxis (anaphylactic or anaphylactoid reaction)

local: grumuloma, hypersensitivity to tuberculin can cause occurrence of vesicles, ulcerations and skin necroses

Although anaphylactic reaction is rare, a proper medical treatment should also always be available following Tuberculin PPD-T application, in order to react immediately to a potential anaphylactic shock.

Overdose

Increase in dose reduces the test specificity and increases the risk of side effects.

Incompatibilities

The preparation must not be mixed with other medicinal products, sera and vaccines in the same syringe.

Shelf-life

Shelf-life is 6 months.

Do not use Tuberculin PPD-T after expiry date on the outer packaging.

Once the vial is opened for the first time, the preparation should be used within 8 hours, provided that it is stored in the refrigerator at 2°C to 8°C.

Special precautions for storage

Store the preparation at 2°C to 8°C in a refrigerator, in the original packaging.

Do not freeze.

Special precautions for disposal of materials to be discarded after the use of Tuberculin PPD-T

Empty vials of tuberculin purified protein derivative for human use, vials which are empty but are not for further use, used syringes, needles and material for disinfection should be disposed of safely in special polyethylene bags and dedicated hard containers, and destroyed in accordance with the current regulations.

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