Package leaflet: Information for the user

BCG 10 Anti-Tuberculosis Vaccine
Powder and solvent for suspension for intradermal injection

Vaccinum tuberculosis (BCG) cryodesiccatum
Vaccine against tuberculosis (BCG), lyophilized
10-dose vaccine

Read all of this leaflet carefully before you start using this vaccine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This vaccine has been prescribed for you only. Do not pass it on to others.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What BCG 10 Anti-Tuberculosis Vaccine is and what it is used for
2. What you need to know before you use BCG 10 Anti-Tuberculosis Vaccine
3. How to use BCG 10 Anti-Tuberculosis Vaccine
4. Possible side effects
5. How to store BCG 10 Anti-Tuberculosis Vaccine
6. Contents of the pack and other information

What BCG 10 Anti-Tuberculosis Vaccine is and what it is used for

BCG 10 Anti-Tuberculosis Vaccine occurs in the form of powder and solvent for the preparation of the suspension for intradermal injections. BCG 10 Anti-Tuberculosis Vaccine contains live attenuated bacteria derived from the culture of Mycobacterium bovis BCG (Bacillus Calmette-Guerin), Moreau substrain.

Vaccine is used for protective vaccinations against tuberculosis.

Vaccinations are mandatory in Poland, carried out in accordance with the Immunization Program Annually approved by the Minister of Health.

Where the child was not vaccinated at birth, vaccination should be performed at the earliest possible date, but no later than before the age of 15 years.

In case of immunisation against tuberculosis booster vaccine doses are not recommended.

What you need to know before you use BCG 10 Anti-Tuberculosis Vaccine

Do not use BCG 10 Anti-Tuberculosis Vaccine:

1. BCG vaccination should not be administered to:
   - persons with known hypersensitivity to any component of the vaccine;
   - neonates of body weight below 2000 g;
   - neonates born to HIV-positive mothers until HIV infection in child can be excluded;
   - neonates with suspected innate immunodeficiency disorders;
   - neonates born to mothers treated in the third trimester of pregnancy with such drugs as monoclonal antibodies against TNF-alpha;
   - HIV-positive persons (confirmed or suspected infections, even if they are asymptomatic);
   - persons with primary or secondary immunodeficiency syndromes (including interferongamma deficiency and DiGeorge syndrome);
   - persons during radiotherapy;
   - persons treated with corticosteroids, in the course of immunosuppressive therapy (including those treated with monoclonal antibodies against TNF-alpha such as, for example: infliximab);
   - persons with cancer (e.g.: leukaemia, Hodgkin's lymphoma, lymphoma or other cancers of the reticuloendothelial system);
   - patients after bone marrow stem cell transplantation and organ transplantation;
   - persons with severe illnesses (including severe malnutrition);

- pregnant women;
- persons who have suffered from tuberculosis or persons with large (over 5 mm) reaction to tuberculin skin test (RT23).

2. Vaccination should be postponed in the case of:
   - clinically unstable neonates until improvement of general state of health (neonates should be vaccinated before leaving the neonatal unit);
   - during infection with fever;
   - exacerbation of a chronic disease;
   - generalised skin infections.

Prematurity as such does not constitute a contraindication to vaccination, vaccination is recommended to be performed in this group of patients after weight gain up to 2000 g.

Warnings and precautions

BCG 10 Anti-Tuberculosis Vaccine should only be administered intradermally.

The potential risk of apnoea and the need for respiratory monitoring for 48–72 h should be considered when administering the vaccine to very premature infants (born ≤ 28 weeks of gestation) and it particularly concerns children with previous history of respiratory immaturity. Due to considerable benefits arising from vaccination of that group of infants, vaccination should not be withheld or delayed.

Vaccination should be postponed in the case of newborns whose mothers have been exposed to antiTNF therapy during pregnancy or other potentially immunosuppressive IgG1 antibodies. A doctor will determine a vaccination date.

Other medicines and BCG 10 Anti-Tuberculosis Vaccine

Intradermal BCG vaccination may be performed concurrently with inactivated or attenuated vaccines. Vaccines containing live microorganisms will not be given at the same time as BCG Vaccine, an interval of not less than four weeks should be allowed to lapse between vaccinations. BCG vaccination should be postponed for four weeks if other live vaccine has been injected. The time interval between vaccine containing live microorganisms and vaccine not containing live microorganisms is optional, maintaining the required interval in order to avoid possible superimposition of adverse postvaccinal reactions to consecutive vaccination.

Other vaccines given at the same time should not be injected in the left arm restricted for the BCG vaccine.

A child should not be vaccinated in the left arm at least for 3 months after administration of BCG due to the risk of regional lymph nodes inflammation.

Pregnancy and breast-feeding

The vaccine should not be administered to pregnant women.
Breastfeeding is not a contraindication to BCG vaccination.

Driving and using machines

BCG 10 Anti-Tuberculosis Vaccine has no or has negligible influence on the ability to drive and use machines.

How to use BCG 10 Anti-Tuberculosis Vaccine

Vaccination should be performed by personnel specially trained in the technique of intradermal injecting.

BCG 10 Anti-Tuberculosis Vaccine should only be administered intradermally!

Description of preparation of BCG 10 Anti-Tuberculosis Vaccine suspension and performance of vaccination is shown under the information destined exclusively for health care professionals, in the latter part of the leaflet.

In accordance with the World Health Organisation recommendations, the BCG Vaccine should be injected in the region of the deltoid muscle of the left upper limb (in the middle part).

Injection of the vaccine into higher region of the arm may lead to keloid formation.
After 2–4 weeks, at the vaccination site in 90-95% of vaccinated individuals an infiltration forms, which remains for several weeks. Predominantly, at the top of the infiltration a pustule and subsequently an ulceration usually 2–5 mm in diameter, not exceeding 10 mm are formed. The lesion is self-healing during 2–3 months from the vaccination leaving a whitish scar several millimetres in diameter. In some persons, out of the pustule serous fluid may ooze for a longer period of time, which is not a complication and does not require treatment but keeping this area clean.

If you use more BCG 10 Anti-Tuberculosis Vaccine than you should

Increase of inoculative dose causes significant increase in the number of post-vaccination complications in the lymph nodes.

Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Lesion at the injection site: infiltration, pustule, ulcerations sometimes with serous fluid drainage usually resolve spontaneously within 3 months from vaccination and does not need treatment. Enlargement of regional lymph nodes, most commonly axillary up to 15 mm in the vaccinated person is considered as an expected normal post-vaccinal reaction.

Severe local reactions such as

- large ulceration (of more than 1 cm in diameter),
- abscess or keloid,

are most commonly connected with a mistake in the vaccine administration technique, incorrect dosage or individual reaction (e.g. positive result of tuberculin skin test - RT23).

If following BCG vaccination local reaction occurs within 24-48 hours and abscess (within 5-7 days), one can suspect previous tuberculosis infection.

Injection of the vaccine too high, in the upper region of the deltoid muscle increases risk of keloid occurrence.

In case of serious local reactions or regional lymph nodes inflammation, medical consultation is required, then an individual decision is made how to proceed, but most commonly no treatment is performed because reactions resolve spontaneously.

Serious systemic reactions following BCG vaccine administration are very rare (approx. 2/1,000,000), and in general affect people with impaired immunity.

Disseminated BCG infection requires expert advice, bacteriological and immune system diagnostics and antimycobacterial treatment in a hospital setting only.

In the case of post vaccination changes occurrence, which according to paediatrician meet criteria of post vaccination complications, a child should be referred to a consultant who will make the final diagnosis and recommend further action.

In preterm infants (born in 28 week of pregnancy or earlier), during 2-3 days following vaccination, longer intervals between breaths may occur.

Tabulated list of side effects

The table below was prepared in accordance with the MedDRA System organ class (system organ class and recommended terminology).

The frequency has been determined according to the following criteria: very common (>1/10), common (>1/100, <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	Side effects	Frequency
Infections and infestations	Pustule/purulent pustule at the injection site	Not known (cannot be estimated from the available data)
	Abscess at the injection site	
	Generalized BCG infection with osteitis	
	Osteomyelitis	
Blood and lymphatic system disorders	Lymph node pain	
	Lymph node necrosis	
	Lymph node enlargement	
	Lymphadenitis /Purulent Lymphadenitis	
Psychiatric disorders	Anxiety	
Respiratory, thoracic and mediastinal disorders	Apnoea in very immature preterm infants (born ≤ 28 week of pregnancy)	
Skin and subcutaneous tissue disorders	Keloid	
General disorders and administration site conditions	Fever	
	Ulceration at the injection site	

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects

directly via the Pharmacovigilance Department of the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products.

02-222 Warszawa, Al. Jerozolimskie 181C tel 22 49 21 301 fax 22 49 21 309 e-mail ndl@urpl.gov.pl

By reporting side effects you can help provide more information on the safety of this medicine.

How to store BCG 10 Anti-Tuberculosis Vaccine

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the packaging. The expiry date refers to the last day of that month.

Store the vaccine in a refrigerator (2ºC - 8ºC). In order to protect the ampoules or vials from light store them in the outer packaging.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

Batch number (Lot)
Expiry date (EXP)

6. Contents of the pack and other information

What BCG 10 Anti-Tuberculosis Vaccine contains
The active substance are live BCG bacilli (Bacillus Calmette-Guerin), the Brazilian Moreau substrain.

One dose (0.1 ml) contains:

50 micrograms (from 150,000 to 600,000) of the semi-dry mass of BCG bacilli.

One ampoule or vial with the powder (10 doses) contains:
0.5 mg (from 1.5 million to 6 million) of live BCG bacilli.
- The excipient is: sodium glutamate One ampoule with solvent contains:

isotonic solution of sodium chloride 1.0 ml.

What BCG 10 Anti-Tuberculosis Vaccine looks like and contents of the pack

Before reconstitution powder in the ampoule or vial is dry amorphous white or light-cream coloured. After reconstitution a homogenous, slightly opalescent suspension without possible presence of flocs or precipitates.

Vaccine should be used directly after reconstitution.

Packaging

5 ampoules with powder and 5 ampoules with solvent of volume of 1 ml
1 ampoule with powder and 1 ampoule with solvent of volume of 1 ml
5 vials with powder and 5 ampoules with solvent of volume of 1 ml
1 vial with powder and 1 ampoule with solvent of volume of 1 ml

Marketing Authorisation Holder and Manufacturer

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Information destined exclusively for health care professionals

Before administering the vaccine the following should be checked on the label: the type of vaccine, the quantity of doses on the ampoule or vial and the expiry date. Furthermore, it should be checked and made sure that the vaccine in the form of a dry powder and is located in full at the bottom of the ampoule or vial.

The neck of the ampoule with the solvent and the ampoule with the powder should be before and after incision as well as the vial before and after removing the plastic cap, precisely disinfected with a swab moistened with 70 % ethyl alcohol and it should be waited until dry.

After opening the ampoule or piercing the rubber stopper of the vial with the powder transfer, by means of a syringe, exactly 1 ml of the isotonic solution of sodium chloride.

The solvent should be poured with a gentle stream alongside the wall of the ampoule or vial.
Next, draw the entire content into a syringe and delicately pour it back to the ampoule or vial avoiding foaming. Repeat this action until a homogenous suspension is obtained. Suspension drawn into a syringe should be homogenous, slightly opalescent.

It is recommended to inspect vaccine visually both before and after its reconstitution in order to avoid the risk of possible presence of flocs or precipitates.

The vaccine should be administered just after its reconstitution.
Aspirate to the syringe only 1 vaccine dose of 0.1 ml for one child.
The injection must be made with a special tuberculin syringe with a well-fitted needle.
Before vaccination, disinfect the skin in the site of administration with alcohol and allow it to dry. Grasp the skin with a thumb and a forefinger of one hand, and insert

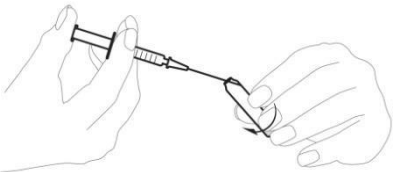
the needle obliquely to a depth of approximately 2 mm below the outer layer of the skin, almost collaterally to its surface. The vaccine should be injected intradermally into the outer 1/3 upper part of the left arm. After administration of 0.1 ml of BCG Vaccine and upon the correct injection technique, an intradermal wheal of approx. 7 mm diameter should be formed.

Remarks:

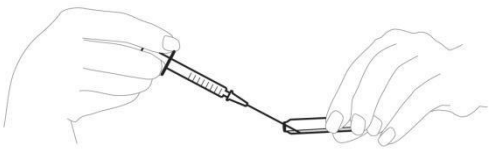
1. All activities related to opening of the ampoules or piercing of the stopper of the vials, transfer of the solvent and vaccine reconstitution should be performed so as to avoid its contamination.
2. For BCG vaccination use only disposable needles and syringes.
3. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Instruction of preparation of BCG 10 Anti-Tuberculosis Vaccine suspension

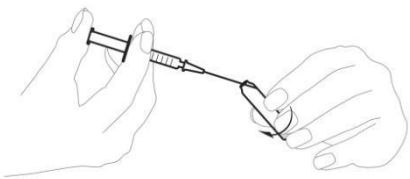
<u>Correct preparation of the BCG 10 Anti-Tuberculosis Vaccine suspension:</u>

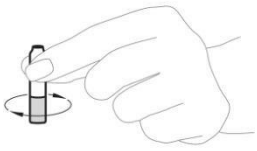


1. Once the ampoule is opened add the solvent with a gentle stream onto the upper wall of the ampoule rotating it gently.



2. Aspirate the whole content to the syringe avoiding foaming and shaking.





3. Pour the contents back to the ampoule with a gentle stream onto the upper wall of the ampoule rotating it gently.

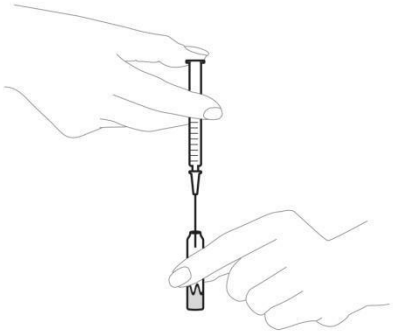
Avoid shaking and foaming.

4. Mix the suspension in the ampoule with a gentle circular movement.

5.Repeat steps 2 through 4 to obtain a homogenous

suspension.

Incorrect preparation of BCG 10 AntiTuberculosis Vaccine suspension:



Do not pour the solvent with a powerful jet into the ampoule!

Do not shake!

Avoid foaming of the suspension in the ampoule.

As a result of shaking and foaming precipitates and flocs may form.

Correct proceeding allows to obtain a homogenous suspension of BCG 10 Anti-Tuberculosis Vaccine.

When flocks or precipitations are formed, discard the ampoule/vial.

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