

SUMMARY OF MEDICINAL PRODUCT CHARACTERISTIC

1. NAME OF THE MEDICINAL PRODUCT

BCG 10 Anti-Tuberculosis Vaccine

Powder and solvent for suspension for intradermal injections

Vaccinum tuberculosis (BCG) cryodesiccatum

Vaccine against tuberculosis (BCG), lyophilised

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One dose (0.1 ml) contains 50 micrograms of semi-dry mass of BCG bacilli which corresponds to amount from 150 000 to 600 000 of live BCG bacilli (*Bacillus Calmette-Guerin*), the Brazilian Moreau substrain.

One ampoule or vial with the powder contains:

0.5 mg (from 1.5 mln to 6 mln) of live BCG bacilli (*Bacillus Calmette-Guerin*), the Brazilian Moreau substrain.

10-dose vaccine

For excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for suspension for intradermal injections.

Before reconstitution powder in the ampoule or vial is dry amorphous white or light-cream coloured.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

BCG 10 Anti-Tuberculosis Vaccine is used for protective vaccinations against tuberculosis.

Catch-up (supplementary) vaccinations in subjects unvaccinated after birth should be performed as early as possible, no later than at 15 years of age.

In case of BCG immunisation booster vaccine doses are not recommended.

4.2 Posology and method of administration

Posology

Solve BCG 10 Anti-Tuberculosis Vaccine in 1 ml of isotonic saline. After reconstitution a homogenous, uniform suspension without possible presence of flocs or precipitates is formed. Aspirate to the syringe only 1 vaccine dose of 0.1 ml for one child.

Method of administration

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

The vaccine should be injected intradermally into the outer 1/3 upper part of the left arm.

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.

After administration of 0.1 ml of BCG Vaccine and upon the correct injection technique, an intradermal wheal approx. 7 mm diameter should be formed.

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.

Instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

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 interferon-gamma 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 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.

4.4 Special warnings and precautions for use

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 \leq 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.

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

4.5 Interaction with other medicinal products and other forms of interaction

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 site postvaccinal effects 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.

4.6 Fertility, pregnancy and lactation

Pregnancy

The vaccine should not be used administered to pregnant women.

Breastfeeding

Breastfeeding is not a contraindication to BCG vaccination.

4.7 Effects on ability to drive and use machines

BCG 10 Anti-Tuberculosis Vaccine has no nor has negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Like all medicines, BCG 10 Anti-Tuberculosis Vaccine may cause adverse reactions. 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 RT23 test).

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.

Respiratory, thoracic and mediastinal disorders

Apnoea in very immature preterm infants (born \leq 28 week of pregnancy - see section 4.4).

Tabulated list of adverse reactions

The table below was prepared in accordance with the MedDRA System Organ Classes classification (System Organ Classes 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 (frequency cannot be estimated from the available data).

MedDRA System Organ Classes	Adverse reactions	Frequency
Infections and infestations	Pustule/purulent pustule at the injection site	Unknown (the frequency can not be determined on the base of 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	
	Lymph node inflammation/ Purulent lymph node inflammation	
Psychiatric disorders	Anxiety	
Respiratory, thoracic and mediastinal disorders	Apnoea in very immature preterm infants (born \leq 28 week of pregnancy)	

Skin and subcutaneous tissue disorders	Keloid	
General disorders and administration site conditions	Fever	
	Ulceration at the injection site	

Reporting of 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 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

web page: <https://smz.ezdrowie.gov.pl>

Adverse reactions can also be reported to the Marketing Authorisation Holder.

4.9 Overdose

Increasing the vaccination dose causes a significant increase in the number of post-vaccination complications in lymphatic nodes.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacological properties

Pharmacotherapeutic group: Vaccine against tuberculosis, live, attenuated,

ATC code: J07AN01

5.2 Pharmacokinetic properties

Following injection, BCG bacilli proliferate at the injection site and in locoregional lymph nodes. The body's response to the presence of bacilli involves development of the delayed-type hypersensitivity, called tuberculin allergy, as well as development of anti-tuberculosis resistance.

5.3 Preclinical safety data

The findings of general toxicity tests performed on guinea pigs and mice after administration of one human dose, and specific toxicity test – harmlessness for guinea pigs after administration of 100 human vaccine doses (test on the presence of virulent mycobacteria) and the Jensen test of skin sensitivity (test of skin over-reactivity) guarantee safety of the medicinal product.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder:

Sodium glutamate

Solvent:

Isotonic solution of sodium chloride

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

30 months.

Vaccine should be used directly after reconstitution.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).

In order to protect the ampoules or vials from light store them in the outer carton.

6.5 Nature and contents of container

0.5 mg of powder in the ampoule or vial made of glass, type I and 1.0 ml of solvent in the ampoule made of glass, type I, in a cardboard box – packages of 1 or 5.

The vial stopper is made of chlorobutyl or bromobutyl rubber with silicone coating.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of the medicinal product and other handling

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.

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.

7. MARKETING AUTHORISATION HOLDER

Synthaverse S.A.
Uniwersytecka Street No. 10, 20-029 Lublin, Poland
tel 81 533 82 21
fax 81 533 80 60
e-mail info@synthaverse.pl

8. MARKETING AUTHORISATION NUMBER(S)

R/0210

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01.03.1994
Date of last renewal: 29.05.2013

10. DATE OF REVISION OF THE TEXT

10/2023