1. NAME OF THE MEDICINAL PRODUCT

BCG Vaccine (Freeze-Dried),
1 ml (0.1 ml x 10 dose / 0.05 ml x 20 dose)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Live, attenuated BCG Vaccine (Bacillus Calmette Guerin Strain)
Each 0.1 ml contains between: 2 x 10^5 and 8 x 10^5 C.F.U.
Reconstitute with Sodium Chloride Injection
Dose: 0.05 ml, Intradermal for infants under one year old.
: 0.1 ml, Intradermal for children over one year of age and adult.

3. PHARMACEUTICAL FORM

Injectable, Powder for Injection.
BCG Vaccine is a live freeze-dried vaccine derived from attenuated strain of *Mycobacterium bovis* (Bacillus Calmette Guerin Moscow strain 361-I) used for the prevention of tuberculosis. The freeze-dried vaccine is white and crystalline in appearance. It contains Sodium glutamate as stabilizer. The vaccine meets the requirements of W.H.O. when tested by the methods outlined in W.H.O., TRS. 979 (2013).

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

BCG vaccine should be given routinely to all infants at risk of early exposure to tuberculosis. This vaccine should be given soon after the child is born. BCG administered early in life provides high level of protection particularly against severe forms of childhood tuberculosis and tubercular meningitis. In countries with low prevalance of tuberculosis, BCG vaccination should be restricted to high risk groups such as hospital personnel and tuberculin negative contacts of known cases of tuberculosis. The vaccine can be given simultaneously with DTP, DT, TT, Measles, Polio, Hepatitis B, *Haemophilus influenzae* type b, yellow fever vaccines and vitamin A supplementation, but at a separate site.

4.2 Posology and method of administration

The vaccine is intended to be injected strictly via the intradermal route, avoiding the subcutaneous route.
The vaccination dose is 0.05 ml for children under one year of age including the new born and 0.1 ml for children over one year of age and adult of the reconstituted vaccine given intradermally. The

skin should not be cleaned with antiseptic. The vaccine should be preferably given with a tuberculin syringe or 25 G/26 G or 27 G sterile needle and syringe.
Skin testing with tuberculin is not generally carried out before giving BCG, but when performed, those who are found to be positive reactors need not be immunized.

Reconstitution:
Tap the vaccine vial gently so as to get the white and crystalline vaccine powder at the bottom of the vial. BCG vaccine vial of 20 doses (0.05 ml) for infants under one year old /10 doses (0.1 ml) for children over one year of age and adult to be reconstituted by adding the entire content of the supplied container of diluent (Sodium Chloride Injection).
Carefully invert the vial a few times to re-suspend freeze dried BCG. Gently swirl the vial of re-suspended vaccine before drawing up each subsequent dose. The resulting suspension should be homogenous, slightly opaque and colourless. The reconstituted suspension may occasionally show clumps, which is normal characteristic of *Mycobacterium bovis*. Avoid vigorous shaking which may enhance/aggrevate clumps formation. Reconstitute only with diluent provided by manufacturer. Using an incorrect diluent may result in damage to the vaccine and / or serious reactions to those receiving the vaccine. Use immediately after reconstitution. If the vaccine is not used immediately then it must be stored in the dark at 2 - 8 º C for no longer than 6 hours (1 immunisation session).
Any opened vial remaining at the end of a vaccination session (within six hours of reconstitution) must be discarded. The vaccine vial monitor for this type of vaccine is attached to the vial cap and should be discarded when the vaccine is being reconstituted.
The diluent and reconstituted vaccine should be inspected visually for any foreign particulate matter and / or variation of physical aspects prior to administration. In the event of either being observed, discard the diluent or reconstituted vaccine.

Intradermal injection technique
The skin is stretched between thumb and forefinger and sterile needle (25 G/26 G or 27 G) inserted bevel upwards for about 2 mm into superficial layers of the dermis (almost parallel with the surface).
Raised blanched bleb showing tips of hair follicles is a sign of correct injection. The site of injection is at insertion of the deltoid muscle into the humerus. Sites higher on the arm are likely to lead to keloid formation.

4.3 Contraindications
BCG vaccine is contraindicated in hypogamma-globulinemia, congenital immunodeficiency, sarcoidosis, leukaemia, generalised malignancy, HIV infections or any other disorder in which natural immune response is altered, as also those on immunosuppressive therapy, corticosteroids,

radiotherapy. In chronic eczema or other dermatological disease, the vaccine can be given in a healthy area of the skin.
Keloid and lupoid reactions may also occur at the site of injection and such children should not be revaccinated.

4.4 Special warnings and precautions for use

Information of anti-tuberculosis drugs: The Minimum Inhibitory Concentration (MIC) towards the *Mycobacterium bovis* BCG Moscow strain 361-I is indicated in below mentioned table.

Drug	Minimum Inhibitory Concentration (MIC)
Isoniazid	0.5 µg/ml
Streptomycin	1.0 µg/ml
Rifampicin	1.0 µg/ml
Ethambutol	5.0 µg/ml

In case of systemic or persistent local infection with BCG vaccine occurs, expert advice should be taken for the necessary treatment. BCG Moscow strain 361-I is resistant to pyrazineamide.

Special case of children born to HIV seropositive mothers.: The obligatory passage of maternal antibodies of the IgG type through the placenta makes it impossible to interpret the serology of the child until the age of about 9-10 months (persistence of the maternal antibodies has been detected up to 14 months).
It is therefore necessary to wait until the child has been found to be seronegative, as determined by immuno-transfer (Western Blot) with the support, if necessary, of techniques for detecting the viral genome, before confirming that the child is not infected.
If the child is infected, BCG vaccine is contraindicated irrespective of the child's condition, given the potential risk of development of "BCG-itis" in the vaccinated child. The advice of a specialized medical team is required.
Neither absence of BCG scar formation nor negative PPD reaction is indicative of poor BCG uptake. There is no need to repeat BCG inoculation in babies who do not develop BCG scar as advocated in the guidelines of IAP 1996.

Immune deficiency: The vaccine is contraindicated in individuals with cell-mediated immune deficiency.
Individuals known to be infected with human immunodeficiency virus (HIV), either non-symptomatic or symptomatic, should NOT receive BCG vaccine.

4.5 Interaction with other medicinal products and other forms of interaction

The BCG vaccine may be routinely given to any child exposed early to the risk contact with the disease (tuberculosis).

The vaccine can be given simultaneously with DTP, DT, TT, Measles, Polio, Hepatitis B, *Haemophilus influenzae* type b, yellow fever vaccines and vitamin A supplementation, but at a separate site.
In order to avoid possible interactions between several medicinal products, any other ongoing treatment should be systematically reported to your doctor.

4.6 Pregnancy and lactation
There is no indication to vaccinate women during pregnancy. Breast feeding can continue despite vaccination with BCG vaccine.
As a general rule, during pregnancy and breastfeeding, it is always recommended to ask your doctor's advice before using a medicinal product.

4.7 Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects
A local reaction is normal. Following BCG vaccination, 2 to 3 weeks later a papule develops at the site of vaccination and increases slowly in size to a diameter of 4-8 mm in 5 weeks. It then subsides or breaks into a shallow ulcer covered with a crust. Healing occurs spontaneously in 6-12 weeks leaving a permanent, tiny round scar 2-10 mm in diameter. In rare cases an abcess may appear at the point of injection, or satellite adenitis, leading in exceptional cases to suppuration. Exceptional cases of lupus vulgaris at the injection site have been reported. Inadvertent subcutaneous injection produces abscess formation and may lead to ugly scars. A risk of generalised reaction to BCG exists in immunodepressed individuals vaccinated with BCG or living in contact with a vaccinated individual.

4.9 Overdose
No cases of overdose have been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties
Pharmacotherapeutic group: Bacterial Vaccines,
Tuberculosis, live attenuated ATC code: J07AN01
Various clinical trials performed to assess the safety and efficacy of the vaccine proved that the vaccine is safe and efficacious.

5.2 Pharmacokinetic properties
Not applicable for vaccines.

5.3 Preclinical safety data
Not available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Monosodium glutamate, USP-NF is the excipient used in the formulation as a stabilizer.

6.2 Incompatibilities
Not applicable.

6.3 Shelf-life
24 months from the date of last satisfactory potency test, if stored in a dark place at a recommended temperature.

6.4 Special precautions for storage
BCG vaccine (Freeze-Dried) should be stored in dark between +2°C to +8°C. It is even more stable if stored in temperatures as low as -20°C. Protect from light.
The diluent should not be frozen, but should be kept cool.

6.5 Nature and contents of container
BCG Vaccine in 4mL USP Type-I, tubular, amber coloured glass vial with bromobutyl rubber stopper and aluminium flip-off seal.
Diluent i.e. Sodium Chloride Injection B.P. (0.9% w/v), 1 ml in USP Type-I clear glass ampoules)

6.6 Special Precautions for Disposal
Once vaccine has been administered, the injection equipment and vaccine containers should be disposed of according to the standard procedures for medical waste.

7. MARKETING AUTHORISATION HOLDER

Serum Institute of India Pvt. Ltd.
S. No 105-110, Manjari Bk. Pune 412 307, India

8. MARKETING AUTHORISATION NUMBER(S)

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9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10. DATE OF REVISION:

04/2023