SUMMARY OF PRODUCT CHARACTERISTICS-BCG FOR VACCINE

1. Name of the Medicinal Product (Generic Name):

1.1 Product Name - BCG Vaccine (Freeze Dried) IP Live attenuated

1.2 Generic name - Bacillus Calmette - Guerin (*Mycobacterium bovis* - Danish 1331)

1.3 Strength - 2 - 8 × 10^6 CFU / Vial

1.4 Pharmaceutical form - White Lyophilized powder.

2. Qualitative and Quantitative Composition:

2.1 BCG (Bacillus Calmette-Guerin) is freeze dried vaccine derived from attenuated strain of *Mycobacterium bovis*. It is used for the prevention of Tuberculosis.

2.2 The vaccine has to be reconstituted with 1.0 ml of sodium chloride injection (0.9% w/v). After reconstitution, a dose of 0.05ml for children up to 1 month, equivalent to 0.1 to 0.4 million CFU / a dose of 0.1ml for children over 1 month and adults, equivalent to 0.2 to 0.8 million CFU.

2.3 The Vaccine has to be administered intradermally and it contains BCG of Danish 1331 of attenuated strain of *mycobacterium bovis*. The vaccine meets the requirements of W.H.O. and I.P. when tested by the methods outlined in W.H.O., TRS. 979 and I.P.

S.No.	Component	Type of ingredient	Concentration
1.	Bacillus Calmette Guerin (Danish-1331 strain) (bacterial suspension)	Active Ingredient	1 mg / Vial (2 to 8 × 10^6 CFU)
2.	Monosodium Glutamate	Excipient	1.5 % (w/v)

3. Pharmaceutical Form:

3.1 Pharmaceutical form - White Lyophilized powder.

3.2 Strength - 2 - 8 × 10^6 CFU / Vial

4. Clinical Particulars:

4.1 Therapeutic Indications:

Active immunization against tuberculosis. BCG vaccine is to be used on the basis of national official recommendations.

4.2 Posology and method of administration:

- Posology -A dose of 0.05mL / 0.1 ml of the reconstituted vaccine is injected strictly by

the intradermal route.

- BCG Vaccine IP:

On reconstitution with 1.0 of ml 0.9 % w/v sodium chloride injection, each dose of 0.1 ml for adults and children aged over one month and adults contains: 2 to 8 × 10^5 CFU. On reconstitution with 1.0 ml of 0.9 % w/v sodium chloride injection, each dose of 0.05mL for children upto one month of age contains: 1 to 4 × 10^5 CFU.

- **Method of Administration** – The injection site should be clean and dry. If antiseptics (such as alcohol) are applied to swab the skin, they should be allowed to evaporate completely before the injection is made. BCG Vaccine should be administrated by personnel trained in intradermal technique.

  BCG vaccine should be injected strictly intradermally in the arm, over the distal Insertion of the deltoid muscle onto the humerus (approx. one third down the Upper arm), as follows:

  - The skin is stretched between thumb and forefinger.
  - The needle should be almost parallel with the skin surface and slowly inserted bevel upward approximately 2 mm into the superficial layers of the dermis.
  - The needle should be visible through the epidermis during insertion.
  - The injection is given slowly.
  - The injection site is best left uncovered to facilitate healing.
  - BCG Vaccine should be administered with a syringe of 1.0 ml sub-graduated into hundredths of ml (1/100 ml) fitted with a short beveled needle (25 G / 0.50 mm or 26G / 0.45 mm). Jet injectors or multiple puncture devices should not be used to administer the vaccine.

4.3 Contraindications:

- BCG Vaccine should not be administered to individuals known to be hypersensitivity to any component of the vaccine.
- Normally, the vaccination should be postponed in persons with pyrexia or generalized infected skin condition. Eczema is not a contraindication, but the vaccine site should be lesion - free.
- BCG vaccine should not be given to persons receiving systemic corticosteroids or immunosuppressive treatment, including radiotherapy, to those suffering from malignant conditions (e.g. lymphoma, leukemia, Hodgkin's disease or other tumors of the reticulo-

endothelial system), those with HIV infection, including infants born to HIV-positive mothers.

- The reaction to BCG vaccination may be exaggerated in these patients, and a generalized BCG infection is possible.
- BCG vaccine should not be given to patients who are receiving anti- tuberculosis drugs.

4.4 Special Warnings and Precautions for Use:

Although anaphylaxis is rare, facilities for its management should always be available during vaccination. Whenever possible, patients should be observed for an allergic reaction for up to 15-20 minutes after receiving immunization. Injections made too deeply, increase the risk of lymphadenitis and abscess formation.

Use BCG vaccine as prescribed by registered medical practitioner and BCG vaccine should be stored in Dark between 2 to 8ºC. Protect from direct sunlight.

4.5 Interaction with other medicinal products and other form of interactions:

Intradermal BCG vaccination may be given concurrently with inactivated or live vaccines. Other vaccines to be given at the same time as BCG vaccine should not be given into the same arm. It is advisable not to give further vaccination in the arm used for BCG vaccination for 3 months because of the risk of regional lymphadenitis.

4.6 Use in special populations (such as pregnant women, lactating women, pediatric patients, geriatric patients etc.) (Pregnancy and Lactation)

Vaccination of mother is not recommended during pregnancy and lactation period.

4.7 Effects on ability to drive and machine:

BCG Vaccine has no or negligible effect on the ability during drive and machine.

4.8 Undesirable Effects:

The expected reaction to successful vaccination with BCG vaccine includes in duration at the injection site followed by a local lesion that may ulcerate some weeks later and heal over some months leaving a small, flat scar. It may also include enlargement of a regional lymph node to < 1cm.

Undesirable effects of the vaccine include the following:

An excessive response to the BCG vaccine may result in a discharging ulcer. This may be attributable to inadvertent subcutaneous injection or to excessive dosage.The ulcer should be encouraged to dry and abrasion (by tight cloths, for Example) avoided.

Uncommon (>1/1000, <1/100)	Systematic: Headache, fever. Local: Enlargement of regional lymph node >1cm. Ulceration with a discharging ulcer at thesite of injection.
Rare (<1/1000)	Systematic: Disseminated BCG complications as osteitis or osteomyelitis. Allergic reactions, including anaphylactic reactions. Local: Suppurative lymphadenitis, abscessformation.

Expert advice should be sought regarding the appropriate treatment regimen for the management of systematic infections or persistent local infections following vaccination with BCG vaccination.

4.9 Overdose:

Overdose increases the risk of suppurative lymphadenitis and may lead to excessive scar formation and gross over dosage increases the risk of undesirable BCG complications.

5. Pharmacological Properties:

5.1 Mechanism of Action

Vaccination with BCG Vaccine elicits a cell-mediated immune response that confers a variable degree of protection to infection with Mycobacterium Tuberculosis. The duration of immunity after BCG vaccination is not known, but there are some indications of warning immunity after 10 years. Vaccinated persons normally become tuberculin positive after 6 week.

A positive tuberculin test indicates a response of the immune system to prior BCG vaccination or to a mycobacterial infection. However the relationship between the post vaccination tuberculin test reaction and the degree of protection afforded by BCG remains unclear.

5.2 Pharmacodynamics properties

- Pharmacotherapeutic group (ATC code): J 07 AN 01.
- BCG Vaccinated persons usually become tuberculin positive after 6 weeks.
- A positive tuberculin skin test indicates a response of the immune system.
- Moreover, a relationship between the post vaccination tuberculin skin test reaction and the degree of protection afforded by BCG remains unclear.

5.3 Pharmacokinetic properties

Not relevant for BCG Vaccine

6. Preclinical safety data:

6.1 Animal Toxicology or Pharmacology

The non-clinical data reveals no hazard for humans based on the safety assessment conducted during the vaccination. During the follow-up there were no deaths or serious adverse events or adverse events observed and no safety issues emerged during observation period.

7. Description

White Lyophilized Powder

BCG Vaccine is a freeze dried live attenuated Bacillus Calmette - Guerin derived from strain of *Mycobacterium bovis*, Danish 1331strain. It is used for prevention of tuberculosis. It contains Monosodium glutamate as a stabilizer.

8. Pharmaceutical Particulars:

8.1 List of Excipient

S. No.	Name of the excipient	Concentration
1.	Monosodium Glutamate	1.5 % (w/v)

8.2 Incompatibilities

BCG Vaccine should not be mixed with other medicinal product.

8.3 Shelf life

24 months from the date of manufacturing, if the product is rightly stored as recommended in the storage condition. From a microbiological point of view the product should be used immediately after reconstitution.

9. Nature and content of Container

BCG Vaccine is filled in USP Type I Amber colour glass vials with bromobutyl rubber stoppers and aluminium flip off seal.

1.0 ml of diluent Sodium Chloride Injection IP (0.9%w/v) in Type I clear glass ampoule.

9.1 Storage and Handling Instruction

9.1.1. Special Precaution for Storage

The vaccine should be stored at 2 to 8ºC (Before and after reconstitution). Do not freeze. Store in order to protect from direct sunlight.

9.1.2. Special precaution for disposal

Once vaccine has been administered, the syringe and vaccine containers should be disposed of according to the standard procedures for medical waste.

10. Patient Councelling Information

BCG Vaccine (Freeze-dried) is a live attenuated Bacillus Calmette–Guerin and induces active immunity against Mycobacterium tuberculosis.

Only diluent provided with the BCG Vaccine should be used for reconstitution.

The rubber stopper must not be wiped with any antiseptic or detergent. If alcohol is used to swab the rubber stopper of the vial, it must be allowed to evaporate before the stopper is penetrated with the syringe needle.

The vaccine should be visually inspected both before and after reconstitution for any foreign particulate matter and also prior to the administration Using a syringe fitted with a long needle, transfer to the vial the volume of diluent given on the label Carefully invert the vial a few times to resuspend the Freeze-Dried BCG completely. DO NOT SHAKE. Gently swirl the vial of resuspended vaccine before drawing up each subsequent dose. When drawn up into the syringe the vaccine suspension should appear homogeneous, slightly opaque. The vaccine should be used immediately after reconstitution. Any unused vaccine or waste material should be disposed of in accordance with local requirements.

11. Marketing Authorization Holder:

GreenSignal Bio Pharma Private Ltd,

Address: No. 49, Pappankuppam Village, Gummidipoondi, Chennai 601201

Phone No: +91-44-2792-2446

Fax No: +91-44-2792-2436

e-mail: gsbpl@gsbpl.com

12. Market Authorization numbers (s):

The Market Authorization (Form 28 D) received from NRA is **TN00002462** dated 29.12.2017