Attachment – 1

Summary of Product Characteristics

SUMMARY OF PRODUCT CHARACTERISTICS

1. TRADE 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

BCG Vaccine is a live freeze-dried vaccine derived from attenuated strain of *Mycobacterium bovis*. (Bacillus Calmette Guerin) used for the prevention of tuberculosis. 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).

BCG vaccine (Freeze-Dried), 1ml contains of a freeze-dried powder and a diluent for reconstitution (Sodium Chloride Injection).

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

Freeze-dried powder for injection

4. CLINICAL DATA

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. DOSE AND METHOD OF ADMINISTRATION

Dose –The vaccination dose is 0.05 ml of the reconstituted vaccine 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.

Method Of Administration – The vaccine is intended to be injected strictly via the intradermal route avoiding the subcutaneous route.
The skin should not be cleaned with antiseptic. The vaccine should be preferably given with a tuberculin syringe or 25G/26G 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.
Intradermal injection technique
The skin is stretched between thumb and forefinger and sterile needle (25G or 26G) 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. CONTRA-INDICATIONS

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.

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 in 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.

4.4. Special warnings and precautions
As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine.
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.

4.5.Interactions with other medicinal products, other interactions
The BCG vaccine may be routinely given to any child exposed early to the risk contact with the disease (tuberculosis). In order to avoid possible interactions between several medicinal products, any other ongoing treatment should be systematically reported to your doctor.
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.

4.6. 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 doctors advice before using a medicinal product.

4.7.Effects on ability to drive and use machines

No effects on ability to drive and use machines have been observed.

4.8. Adverse reactions

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 case of overdose has been reported.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group : Bacterial Vaccine, ATC code : J07AN 01

BCG vaccine is used to stimulate active immunity to tuberculosis. Because the Calmette-Guerin strain of M. bovis present in BCG vaccine is immunologically similar to M tuberculosis, vaccination with BCG stimulates natural infection with M. tuberculosis and promotes cell-mediated immunity against tuberculosis.

Vaccination with BCG generally results in tuberculin sensitivity, but the degree of tuberculin sensitivity is highly variable and depends partly on the strain of BCG used in the vaccine. The ability of a particular BCG vaccine to cause tuberculin sensitivity has generally been used to indicate its immunizing potential and conversion of the tuberculin skin test following vaccination has generally been used to indicate immunity against tuberculosis. However, the relationship between tuberculin sensitivity following BCG vaccination and immunity against tuberculosis has not been adequately studied to date. Efficacy of the currently available BCG vaccines has not been demonstrated directly and can only be inferred. Although the protection against M. tuberculosis infection afforded by the vaccine is highly variable, diagnostic and clinical evidence has generally demonstrated a reduction in the incidence of tuberculosis in immunized individuals as compared with non-immunized individuals.

The duration of protection against tuberculosis infection following administration of BCG vaccine has not been determined and depends on the potency and dosage of the vaccine used. In several studies, tuberculin sensitivity persisted 7-10 years following

BCG vaccination; however, a definite relationship between tuberculin sensitivity and immunity has not been established.

BCG vaccine and the methanol-extracted residue (MER) of BCG have been shown to be potent stimulators of host defense mechanisms. In animals, BCG increases resistance of the animal to tumor growth following inoculation with tumor cells. There is also evidence of tumor (e.g. malignant melanoma) regression following intralesional injection of BCG vaccine. Inclusion of BCG in tumor antigen-containing vaccines has been reported to enhance induction by the vaccine of a tumor specific immune response. The immunostimulant effect of specific BCG preparations is reportedly variable. The mechanism (s) of BCG's immunostimulant effect has not been fully determined. It is not known whether antibodies or specifically sensitized cells are involved in the antitumor effect of BCG. Antimelanoma antibody titres have increased in patients with melanoma receiving BCG therapy.
Although BCG has been shown to stimulate natural killer-cell (a subpopulation of lymphocytes) activity and macrophage activity, the relation of these effects to the vaccine's antitumor activity has not been established. For BCG to have an antitumor effect, it appears that the tumor host must be immunocompetent, a sufficient dose of BCG must be given, the tumor burden must be relatively low, administered BCG must be closely associated with the tumor cells and the tumor must be immunogenic.

5.2. Pharmacokinetic properties

Pharmacokinetic studies are not required for vaccines.

5.3.Preclinical safety data

Keeping in mind the safety tests done on animals, on each batch of vaccine manufactured and extensive human use of this vaccine, which has proven the safety beyond doubt, the animal toxicity data is not applicable.

6.PHARMACEUTICAL PROPERTIES

6.1. List of Excipients

Monosodium Glutamate.

6.2. Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.
The vaccine can be given simultaneously with DTP, DT, TT, Measles, Polio and Hepatitis B vaccines, but at a separate sites.

6.3. Shelf Life

24 months from date of last satisfactory potency test, if stored in a dark place at a temperature between 2-8°C.

6.4. Special Precautions for storage

Stored and transport between +2°C to +8°C.
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 Packaging

The vaccine is lyophilized and available in amber Type I glass vial with bromobutyl stopper and flip off aluminium cap; 1 ml of diluent in glass ampoule

One vial of reconstituted vaccine contains 1 ml, corresponding to 10 doses (0.1 ml) for children over one year of age and adult or 20 doses (0.05 ml) for infants under one year old.

6.6. Instructions regarding the preparation of medicinal products for its use and handling

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 to be reconstituted with 1 ml of sodium chloride injection.
Carefully invert the vial a few times to resuspend freeze dried BCG. Gently swirl the vial of resuspended vaccine before drawing up each subsequent dose. The resulting suspension should be homogenous, slightly opaque and colourless. 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 should be stored in the dark at 2° to 8°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.

7. MARKETING AUTHORIZATION HOLDER

SERUM INSTITUTE OF INDIA LTD
REGD OFFICE AND LABORATORIES:
212/2, HADAPSAR, PUNE - 411028.
MAHARASHTRA, INDIA.
TELEPHONE: ++ 91-20- 26602363 / 26993900 / 04
FAX: ++ 91- 20-26993924 / 26993921
WEBSITE: www.seruminstitute.com

8. NUMBER IN THE REGISTER OF MEDICINAL PRODUCTS

Manufacturing Licence no. 10 (In form 28D)

9. DATE OF AUTHORIZATION OR LAST RENEWAL OF AUTHORIZATION

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10. DATE OF REVISION OF TEXT
