

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1. NAME OF THE MEDICINAL PRODUCT

BCG Vaccine SSI, powder and solvent for suspension for injection.

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, 1 dose (0.1 ml) for adults and children aged 12 months and over contains: *Mycobacterium bovis* BCG (Bacillus Calmette-Guerin), Danish strain 1331, live attenuated,  $2-8 \times 10^5$  cfu.

After reconstitution, 1 dose (0.05 ml) for infants under 12 months of age contains: *Mycobacterium bovis* BCG (Bacillus Calmette-Guerin), Danish strain 1331, live attenuated,  $1-4 \times 10^5$  cfu.

This is a multidose container. See section 6.5 for the number of doses per vial.

For excipients, see section 6.1

### 3. PHARMACEUTICAL FORM

Powder and solvent for suspension for injection.

White crystalline powder (might be difficult to see due to the small amount of powder in the vial).

The solvent is a colourless solution without any visible particles.

### 4. CLINICAL PARTICULARS

#### 4.1. Therapeutic indications

Active immunisation against tuberculosis.

BCG Vaccine SSI is to be used on the basis of national official recommendations.

#### 4.2. Posology and method of administration

##### Posology:

*Adults and children aged 12 months and over:*

A dose of 0.1 ml of the reconstituted vaccine is injected strictly by the intradermal route.

*Infants under 12 months of age:*

A dose of 0.05 ml of the reconstituted vaccine is injected strictly by the intradermal route.

National recommendations should be consulted regarding the need for tuberculin testing prior to administration of BCG Vaccine SSI.

##### 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 administered by personnel trained in the intradermal technique.

The 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 upwards), 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.
- A raised, blanched bleb is a sign of correct injection.

- The injection site is best left uncovered to facilitate healing.

BCG Vaccine SSI should be administered with a syringe of 1 ml subgraduated into hundredths of ml (1/100 ml) fitted with a short bevel needle (25G/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 SSI should not be administered to individuals known to be hypersensitive to any component of the vaccine.

Normally, the vaccination should be postponed in persons with pyrexia or generalised infected skin conditions. Eczema is not a contraindication, but the vaccine site should be lesion free.

BCG Vaccine SSI should not be given to persons receiving systemic corticosteroids or immunosuppressive treatment including radiotherapy, to those suffering from malignant conditions (e.g., lymphoma, leukaemia, Hodgkin's disease or other tumours of the reticulo-endothelial system), those with primary or secondary immunodeficiencies, those with HIV-infection, including infants born to HIV-positive mothers. The effect of BCG vaccination may be exaggerated in these patients, and a generalised BCG-infection is possible. In areas where the risk of contracting tuberculosis and HIV is high, it may be appropriate to vaccinate asymptomatic HIV-positives with BCG according to WHO recommendations.

BCG Vaccine SSI 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.

Tuberculin positive persons (consult national recommendations for the definition of a positive tuberculin reaction) do not require the vaccine. Administration of the vaccine to such persons may result in a severe local reaction.

Injections made too deeply increase the risk of lymphadenitis and abscess formation.

Regarding undesirable effects caused by BCG-infection and the susceptibility of the strain to anti-tuberculous drugs refer to section 4.8.

#### 4.5. Interactions with other medicinal products and other forms of interaction

Intradermal BCG vaccination may be given concurrently with inactivated or live vaccines, including combined measles, mumps and rubella vaccines.

Other vaccines to be given at the same time as BCG Vaccine SSI should not be given into the same arm. If not given at the same time an interval of not less than four weeks should normally be allowed to lapse between the administrations of any two live vaccines.

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. Pregnancy and lactation

Although no harmful effects to the foetus have been associated with BCG vaccine, vaccination is not recommended during pregnancy or lactation.

However, in areas with high risk of tuberculosis infection, BCG may be given during pregnancy or lactation if the benefit of vaccination outweighs the risk.

#### 4.7. Effects on the ability to drive and use machines

BCG Vaccine SSI has no or negligible influence on the ability to drive and use machines.

#### 4.8. Undesirable effects

The expected reaction to successful vaccination with BCG Vaccine SSI includes

induration 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 also may include enlargement of a regional lymph node to < 1 cm.

Undesirable effects of the vaccine include the following:

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

An excessive response to the BCG Vaccine SSI 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 clothes, for example) avoided.

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

Antibiotic sensitivity of the BCG strain:

Section 5.1 includes a table with minimum inhibitory concentrations (MIC) for selected anti-tuberculous drugs towards the BCG Danish strain 1331 (as determined by Bactec 460).

The MIC for isoniazid is 0.4 mg/l. There is no consensus as to whether *Mycobacterium bovis* should be classified as susceptible, intermediately susceptible or resistant to isoniazid when the MIC is 0.4 mg/l. However, based on criteria set for *Mycobacterium tuberculosis*, the strain could be considered to be of intermediate susceptibility.

#### 4.9. Overdose

Overdose increases the risk of suppurative lymphadenitis and may lead to excessive scar formation. Gross overdosage increases the risk of undesirable BCG complications. For treatment of disseminated infections with BCG, refer to section 4.8.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamic properties

Pharmacotherapeutic group (ATC code): J 07 AN 01. MIC values for selected anti-tuberculous agents against the BCG Danish strain 1331 using the Bactec 460 method are as follows:

Drug	Minimum Inhibitory Concentration (MIC)
Isoniazid	0.4 mg/l
Streptomycin	2.0 mg/l
Rifampicin	2.0 mg/l
Ethambutol	2.5 mg/l

BCG Danish Strain 1331 is resistant to pyrazinamide.

Vaccination with BCG Vaccine SSI elicits a cell-mediated immune response that confers a variable degree of protection to infection with *M. tuberculosis*. The duration of immunity after BCG vaccination is not known, but there are some indications of a waning immunity after 10 years.

Vaccinated persons normally become tuberculin positive after 6 weeks.

A positive tuberculin skin 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 skin test reaction and the degree of protection afforded by BCG remains unclear.

### 5.2. Pharmacokinetic properties

Not relevant for vaccines.

### 5.3. Preclinical safety data

No relevant data available.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of excipients

*Powder:*

Sodium glutamate.

*Solvent:*

Magnesium sulphate heptahydrate

Dipotassium phosphate

Citric acid, monohydrate

L-asparagine monohydrate

Ferric ammonium citrate

Glycerol 85%

Water for injections

### 6.2. Incompatibilities

BCG Vaccine SSI should not be mixed with other medicinal products.

### 6.3. Shelf life

18 months.

From a microbiological point of view the product should be used immediately after reconstitution. In use stability in terms of viability has been demonstrated for 4 hours after reconstitution.

### 6.4. Special precautions for storage

Store in a refrigerator (2°C - 8°C).

Do not freeze. Store in original package in order to protect from light.

### 6.5. Nature and contents of container

Powder in amber Type I glass vial with bromobutyl stopper and aluminium cap; 1 ml of solvent in Type I glass vial with a chlorbutyl stopper and an aluminium cap.

Packages of 1, 5, 10 vials and a 1 vial presentation including 1 unidose injection kit (one polypropylene syringe and two injection needles (one long for adding solvent and one short for intradermal injection)).

One vial of reconstituted vaccine contains 1 ml, corresponding to 10 doses for adults and children aged 12 months and over (0.1 ml) or 20 doses for infants under 12 months of age (0.05 ml).

Not all pack sizes may be marketed.

### 6.6. Instruction for use and handling

*Reconstitution:*

Only solvent 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 prior to the administration.

Using a syringe fitted with a long needle, transfer to the vial the volume of solvent given on the label. Carefully invert the vial a few times to resuspend the lyophilised 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 and colourless.

From a microbiological point of view the product should be used immediately after reconstitution. In use stability in terms of viability has been demonstrated for 4 hours after reconstitution.

Any unused vaccine or waste material should be disposed of in accordance with local requirements.

**7. MARKETING AUTHORIZATION HOLDER**

Statens Serum Institut  
5, Artillerivej  
DK-2300 Copenhagen S.

**8. MARKETING AUTHORIZATION NUMBER**

**9. DATE OF FIRST AUTHORIZATION**

9 September 1993

**10. DATE OF REVISION OF THE TEXT**