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-Guérin), Danish strain 1331, live attenuated, 2-8 x 10^5 cfu.

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

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

For the full list of 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 immunization against tuberculosis.

4.2 Posology and method of administration

Posology:
Children at least 12 months of age and adults:
0.1 ml of the reconstituted vaccine strictly by intradermal injection.

Infants under 12 months of age:
0.05 ml of the reconstituted vaccine strictly by intradermal injection.

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

Method of Administration:
BCG VACCINE SSI should be administered with a syringe fitted with a short bevel needle (25G/ 0.50 mm or 26G/0.45mm).
BCG VACCINE SSI should be administered by personnel trained in the intradermal technique.

Jet injectors or multiple puncture devices should not be used to administer the vaccine.
The injection site should be clean and dry; Antiseptics should not be used prior to administration. If alcohol is used to swab the skin, it must be allowed to evaporate before the vaccine is injected. 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.

For instructions on reconstitution of the vaccine before administration, see section 6.6

4.3 Contraindications

BCG VACCINE SSI should not be administered to persons known to be hypersensitive to the active substance or to any of the excipients listed in section 6.1.

Vaccination should be postponed in persons suffering from acute severe febrile illness or with generalised infected skin conditions. Eczema is not a contraindication, but the vaccine site should be lesion free.

BCG VACCINE SSI should not be administered to persons in treatment with systemic corticosteroids or immunosuppressive treatment including radiotherapy. This also includes infants exposed to immunosuppressive treatment in utero or via breastfeeding, for as long as a postnatal influence of the immune status of the infant remains possible (e.g. maternal treatment with TNF-α antagonist). In persons whose immune status is in question, the BCG vaccine should be postponed until the immune status has been evaluated. Furthermore BCG VACCINE SSI should not be given to persons 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.

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, vaccinated persons should be observed for an allergic reaction for up to 20 minutes after immunisation. 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.

Administering the vaccine too deep increases the risk of discharging ulcer, lymphadenitis and abscess formation.

Cases of Immune reconstitution inflammatory syndrome (IRIS) have been reported after the onset of antiretroviral therapy in HIV-infected children or after initiating treatment for other severe immune deficiencies in children who had prior BCG vaccination. Adenitis, suppurative adenitis, purulent discharge, skin ulceration, skin abscesses, fever, have been reported in association with IRIS, appearing within weeks to months after initiation of immune therapy. Clinicians should be aware of this syndrome when treating patients with primary or secondary immunodeficiency who had prior BCG vaccination.

BCG VACCINE SSI should under no circumstances be administered intravascularly.
The vaccine contains less than 1 mmol sodium (23 mg) per dose and is essentially free of sodium.

4.5 Interaction with other medicinal products and other forms of interactions

BCG may be given simultaneously, at a separate site, with all other vaccines and immunoglobulins.

Intradermal BCG vaccination may be given concurrently with inactivated killed or live vaccines, including combined the 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.

No further vaccination should be given for at least three months in the arm used for BCG vaccination, because of the risk of regional lymphadenitis.

4.6 Fertility, pregnancy and lactation

Pregnancy
Although no harmful effects to the foetus have been associated with BCG VACCINE SSI, vaccination is not recommended during pregnancy.

Breastfeeding
Although no harmful effects to the child have been associated with BCG VACCINE SSI, vaccination of the mother is not recommended during lactation.

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

Fertility
No clinical or non-clinical data are available on the possible effects of BCG VACCINE SSI on male and female fertility.

4.7 Effects on 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 < 1cm.

Undesirable effects of the vaccine include the following:

	Uncommon (≥1/1000 to <1/100)	Rare (≥1/10000 to <1/1000)
Blood and Lymphatic system disorder	Enlargement of regional lymph > 1 cm	
Nervous system disorder	Headache	
Muscoloskeletal and connective tissue disorders		Osteitis
Infections and infestations	Suppurative lymphadenitis	Osteomyelitis Injection site abscess
General disorders and administration site conditions	Fever Injection site ulceration Injection site discharge	
Immune system disorders		Anaphylactic reactions Allergic reactions

During post-marketing safety surveillance syncope among patients receiving injections have been reported. Also seizures and convulsions have been reported infrequently.

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.

Localised or disseminated infection with *M. bovis* BCG can occur in rare cases upon BCG vaccination. Expert advice should be sought regarding the appropriate treatment regimes for systemic infections or persistent local infections following vaccination with BCG VACCINE SSI.

Reporting of suspected 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

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.

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.

The duration of immunity after BCG vaccination is not known, but there are some indications of a waning immunity after 10 years.

BCG Danish strain 1331 is susceptible to most commonly used anti-tuberculous drugs. However the MIC of isoniazid for the BCG Danish strain 1331 is 0.4 mg/ml [Bactec 460]. There is no consensus as to whether *M bovis* should be classified as susceptible, intermediately resistant or resistant to isoniazid when MIC is 0.4mg/ml. However, based on criteria set for *Mycobacterium tuberculosis,* the strain could be considered to be of intermediate susceptibility.

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.

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

BCG VACCINE SSI SSI:
Sodium L-glutamate monohydrate

Diluted Sauton SSI:
Magnesium sulphate heptahydrate
Dipotassium phosphate
Citric acid, monohydrate
L-asparagine monohydrate
Ferric ammonium citrate
Glycerol 85%
Water for injections

6.2 Incompatibilities

Only Diluted Sauton SSI may be used for reconstitution of BCG VACCINE SSI. In the absence of compatibility studies BCG VACCINE SSI must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

2 years

From a microbiological point of view the vaccine 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.

For storage conditions after reconstitution of the vaccine, see section 6.3.

6.5 Nature and contents of container

Nature and content:

BCG VACCINE SSI in amber Type I glass with bromobutyl stopper and aluminium cap; 1 ml of Diluted Sauton SSI in Type I glass vial with a chlorbutyl stopper and an aluminium cap.

5 vials BCG VACCINE SSI (0.75 mg BCG) + 5 vials Diluted Sauton SSI (1 ml) packed in the same box.

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).

6.6 Special precautions for disposal and other handling

Reconstitution:
Only Diluted Sauton SSI provided with the BCG VACCINE SSI 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 Diluted Sauton 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 vaccine should be used immediately after reconstitution.

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

7 MARKETING AUTHORISATION HOLDER

AJ Vaccines A/S
5 Artillerivej
DK-2300 Copenhagen S
Denmark

8 MARKETING AUTHORISATION NUMBER

PA2160/003/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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