SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

BCG Vaccine AJV, 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 x 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 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 immunisation against tuberculosis.

BCG Vaccine AJV 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 AJV.

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 AJV 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.

For information on the expected reaction following successful vaccination with BCG Vaccine AJV, see section 4.8.

BCG Vaccine AJV 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.

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

4.3 Contraindications

BCG Vaccine AJV should not be administered to individuals known to be hypersensitive to the active substance or to any 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 AJV should not be administered to persons in treatment with systemic corticosteroids or other 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 antagonists).

Furthermore BCG Vaccine AJV 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 immune-deficiencies, those with HIV-infection, including infants born to HIV-positive mothers.

In persons whose immune status is in question, the BCG vaccination should be postponed until the immune status has been evaluated.

The effect of BCG vaccination may be exaggerated in immunosuppressed patients, and a generalised BCG-infection is possible.

BCG Vaccine AJV 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.

Administering the vaccine too deep increases the risk of discharging ulcer, lymphadenitis and abscess formation. See section 4.2 for method of administration.

BCG Vaccine AJV should under no circumstances be administered intravascularly.

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

The potential risk of apnoea and the need for respiratory monitoring for 48–72 h should be considered when administering the primary immunisation series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity.

As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed.

BCG Vaccine AJVaccines contains less than 1 mmol of potassium (39 mg) and sodium (23 mg) per dose and is essentially free of potassium and sodium.

4.5 Interaction 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 AJV 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 Fertility, pregnancy and lactation

Pregnancy

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

Breastfeeding

Although no harmful effects to the breastfed child have been associated with BCG Vaccine AJV, vaccination of the mother is not recommended during lactation.

However, in areas with high risk of tuberculosis infection, BCG Vaccine AJV 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 AJV on male or female fertility.

4.7 Effects on ability to drive and use machines

BCG Vaccine AJV 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 AJV 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.

A local site reaction may include erythema and tenderness.

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

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 node > 1 cm	-
Nervous system disorder	• Headache	-
Musculoskeletal 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 reaction • Allergic reaction

Apnoea in very premature infants (born ≤ 28 weeks of gestation) (see section 4.4).

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

An excessive response to the BCG Vaccine AJV 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 AJV.

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.

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

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 AJV 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 AJVaccines should not be mixed with other medicinal products except those mentioned in section 6.6.

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 ºC – 8 ºC).
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

Powder in amber Type I glass vial with bromobutyl stopper and aluminium cap; 1 ml of solvent in Type I glass vial with a chlorobutyl 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 Special precautions for disposal

Reconstitution:

Only solvent provided with the BCG Vaccine AJV 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 AUTHORISATION HOLDER

AJ Vaccines A/S
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DK-2300 Copenhagen S
Denmark

8 MARKETING AUTHORISATION NUMBER(S)

PL 46796/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9 September 2002

Date of latest renewal: 26 October 2007

10 DATE OF REVISION OF THE TEXT

22/05/2018