

BCG Vaccine

For Intradermal Injection

Name of the medicine

BCG VACCINE, Bacillus Calmette and Guérin

Description

BCG Vaccine (Bacillus Calmette-Guérin) is a freeze-dried live bacterial vaccine prepared from an attenuated strain of *Mycobacterium bovis*. When reconstituted as directed with the accompanying phosphate buffered saline diluent, the vaccine contains between 8×10^6 and 32×10^6 colony forming units per mL of product and monosodium glutamate 1.5% w/v.

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|---------------------|------------------------------|-------------|
| Active ingredients: | Bacillus Calmette and Guérin | 1.5 mg |
| Excipients: | monosodium glutamate | 1.5% w/v |
| Diluent: | sodium chloride | 0.85% |
| | sodium phosphate - dibasic | 0.25% |
| | sodium phosphate - monobasic | 0.06% |
| | polysorbate 80 | 0.025% |
| | water for injection | q.s. 1.5 mL |

This vaccine does not contain added preservative.

This vaccine fulfils WHO requirements for Dried BCG Vaccine.

Pharmacology

Clinical studies have demonstrated that BCG vaccine induces a cell-mediated immune response (tuberculin positive skin reaction) in at least 90% of adult recipients. The development of this response takes several weeks. Clinical trials have not shown a consistent relationship between the size of tuberculin reactions and the protection provided by BCG vaccines.

Two retrospective case control studies in Aboriginal Canadian Indians have shown that Sanofi Pasteur Limited's BCG Vaccine provides approximately 60% protective efficacy.

Indications

BCG Vaccine is indicated for active immunisation against tuberculosis.

Administration of BCG Vaccine (Freeze-Dried) is recommended for individuals:

- who comprise a group in which an excessive rate of infections can be demonstrated. (Such groups might exist among those without a regular source of healthcare.) or
- who are repeatedly exposed to persistently untreated or ineffectively treated patients with sputum-positive pulmonary tuberculosis, or
- who are health workers at increased risk of repeated exposure, especially those working in institutions serving major urban population centres in which the endemic prevalence of tuberculosis is relatively high.

BCG Vaccine should be administered to all infants at risk of early exposure to the disease.

Contraindications

Allergy to any component of BCG Vaccine including monosodium glutamate and polysorbate 80 or an anaphylactic or other allergic reaction to a previous dose of BCG vaccine are contraindications to vaccination.

Individuals who have previously had tuberculosis or who have a positive tuberculin reaction of over 5 mm.

Individuals with significant fever. Immunisation with BCG Vaccine should be deferred during the course of a moderate or severe febrile illness or acute infection to avoid superimposing potential adverse effects of the vaccine on the underlying illness.

Individuals with generalised skin disease such as eczema, furunculosis, atopic dermatitis or other exudative or inflammatory dermatologic conditions.

Keloid and lupoid reactions may occur at the site of injection. This should be considered in deciding whether to vaccinate individuals predisposed to such reactions.

BCG vaccine should not be administered to individuals with known natural or acquired immunodeficiency conditions or those receiving immunosuppressant therapy because of the risk of disseminated BCG infection in those individuals. BCG Vaccine should not be administered to individuals with a high risk of HIV infection where HIV antibody status is unknown.

Precautions

The stopper of the vial for this product contains dry natural latex rubber. Natural latex rubber has been associated with allergic reactions.

BCG Vaccine contains viable attenuated mycobacteria and should be handled as potentially infectious. All equipment and material used during reconstitution and

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subsequent immunisation should be handled and disposed of as biohazardous material.

BCG vaccination is a preventative measure, and has no value in the treatment of tuberculosis. BCG immunisation will not prevent the development of active tuberculosis in individuals who are already infected with *Mycobacterium tuberculosis*.

As with most vaccines, vaccination will not protect 100% of susceptible individuals.

This presentation of BCG Vaccine is not a treatment for carcinoma in-situ of the urinary bladder.

If a tuberculin skin test has been carried out, those who develop positive reactions should not be immunised (see Contraindications).

Do not combine BCG Vaccine in the same syringe as other vaccines (see Interactions with other medicines).

Effects on fertility

It is not known whether BCG Vaccine can affect reproduction capacity

Use in Pregnancy (Category B2)

There is no convincing evidence of the risk to the foetus from immunisation of pregnant woman using bacterial vaccines. Although no harmful effects of BCG Vaccine on the foetus have been observed, vaccination of women during pregnancy is not recommended unless there is an excessive risk of unavoidable exposure to infective tuberculosis.

Use in lactation

It is not known whether BCG Vaccine is excreted in human milk. Because live vaccines may be excreted in human milk, caution should be exercised when BCG Vaccine is administered to a nursing woman.

Paediatric use

See Dosage and administration.

Use in the elderly

Clinical experience with BCG Vaccine in the elderly is limited.

Genotoxicity

No genotoxicity studies have been conducted with BCG Vaccine.

Carcinogenicity

No carcinogenicity studies have been conducted with BCG Vaccine.

Effect on laboratory tests

Inteference of BCG Vaccine with laboratory tests has not been studied.

Interactions with other medicines

BCG Vaccine must not be combined with other vaccines in the same syringe; however, it may be administered at the same time as other vaccines provided they are injected SEPARATELY and at different sites. A 4 week interval between administration of BCG vaccine and other live vaccines is recommended.

Adverse effects

Response to BCG vaccination

General disorders and administration site conditions

Following intradermal vaccination a red, small indurated papule (measuring 5 – 15 mm in diameter) appears within 1 to 3 weeks. The papule tends to soften and break down, resulting in a small ulcer in the majority of subjects. The ulcers heal over a number of weeks, usually leaving a superficial scar.

Some enlargement of the regional lymph nodes may accompany the lesion at the vaccination site. This was observed in 25% of subjects in a study in newborn infants. Spontaneous regression usually occurs within a few months. If abscesses of the lymph nodes develop, they should be punctured (aspirated) only if they are soft and fluctuating. Antituberculous chemoprophylaxis should be considered. **Surgical incision or excision of the lymph nodes is not recommended.**

In studies of BCG Vaccine ulceration of > 5 mm at the site of intradermal vaccination is the most common adverse reaction observed (35 – 69% of subjects).

In some cases, a cold abscess may appear at the site of injection. Spontaneous resorption usually occurs.

Inadvertent subcutaneous injection may result in abscess formation and may lead to ugly retracted scars.

Gross local or generalised infections should be treated with antituberculous chemotherapy.

Disseminated *Mycobacterium bovis*, var BCG, infection occurred in four Aboriginal Canadian infants who had been immunised with BCG Vaccine in the neonatal period. All cases were in infants with immunodeficiencies (including severe combined immunodeficiency, HIV/AIDS, defect in interferon gamma) which had not been detected before immunisation.

Disseminated BCG infection has been reported rarely after BCG vaccination, principally in immunocompromised individuals. In some cases deaths have been associated with disseminated BCG infection.

Anaphylactoid reactions have been reported rarely following administration of BCG Vaccine. Keloid formation and cutaneous reactions such as erythema nodosum have also been reported after BCG vaccination.

Regional (e.g. axillary) lymphadenopathy follows BCG vaccination (various strains from various manufacturers) with a frequency ranging from 1 – 10%. Suppurative lymphadenitis is much less common than lymphadenopathy, occurring in 0.03 – 0.5% of BCG vaccine recipients. Multiple lymphadenitis, hepatomegaly, splenomegaly and other nonfatal disseminated lesions have occurred at rates of 0.31 to 0.39 per 1 million vaccinations.

One case of osteomyelitis associated with BCG Vaccine was reported in 1998. Osteitis has been observed mostly in Scandinavian countries, possibly related to the strain used. The risk for developing osteitis after BCG vaccination varies by country.

Dosage and administration

The dose of the reconstituted vaccine:

- **In newborns and infants up to 12 months of age, 0.05 mL**
- **In children over 12 months of age and adults, 0.1 mL**

The freeze-dried vaccine is reconstituted using the accompanying diluent.

Reconstitution of Freeze-Dried Vaccine and Withdrawal from Rubber Stopped Vial

- Do not remove the rubber stopper from the vial.
- Apply a sterile piece of cotton moistened with a suitable antiseptic to the surface of the rubber stopper of the vial of vaccine.
- Withdraw the diluent (**1.5 mL**) into a syringe.
- Holding the plunger of the syringe containing the diluent steady, pierce the centre of the rubber stopper in the vial and inject the required volume of diluent (**1.5 mL**) into the freeze-dried vaccine.
- Do not try to force all of the diluent into the vial at once as this will create pressure. It is important to allow air to escape into the syringe by intermittently aspirating air from the vial while injecting the diluent into the vial.
- Holding the syringe plunger steady, withdraw the needle from the vial.
- Shake the vial gently until a fine, even suspension results. **Avoid foaming** as this will prevent withdrawal of the proper dose.
- Using a 1.0 mL sterile syringe with a 26-gauge needle, inject 0.1 mL (0.05 mL for newborns and infants up to 12 months of age) of the reconstituted vaccine for injection **intradermally** into the most superficial layers of the skin at one site. The bevelled side of the needle should face upwards.

BCG Vaccine must be administered intradermally. **DO NOT ADMINISTER SUBCUTANEOUSLY, INTRAMUSCULARLY OR INTRAVENOUSLY.**

A SEPARATE STERILE NEEDLE AND SYRINGE MUST BE USED FOR EACH INDIVIDUAL PATIENT.

After reconstitution with the diluent supplied, store at 2°C to 8°C. Any reconstituted vaccine not used within 8 hours **MUST** be discarded using methods suitable for biohazardous material. Any reconstituted product which exhibits flocculation or clumping that cannot be dispersed with gentle shaking should not be used.

Revaccination

When BCG vaccination is followed by positive tuberculin response, there is no current indication that revaccination is necessary within 5 to 10 years.

In areas where young children are vaccinated, a second vaccination is sometimes given between the ages of 12 to 15 years to those with a negative tuberculin reaction.

Overdosage

The recommended dosage for age should not be exceeded, as this may result in more extensive local reactions. Subcutaneous or intramuscular injection may result in an abscess at the injection site.

Presentation and storage conditions

Presentation

Multidose vial containing 1.5 mg of lyophilised vaccine, with accompanying 1.5 mL of diluent. When reconstituted, this is enough to provide for 10 adult doses or 20 infant doses.

Storage

Store at 2° to 8° C. Refrigerate. Do not freeze. Protect from light. At no time should the freeze-dried or reconstituted vaccine be exposed to sunlight, direct or indirect. Exposure to artificial light should be kept to a minimum.

Medicine classification

Prescription Medicine

Name and address of the sponsor

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BCG VACCINE Data Sheet

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