Public Health England

TO MEMBERS OF THE MEDICAL, NURSING, MIDWIFERY AND PHARMACEUTICAL PROFESSIONS

IMPORTANT – PLEASE READ: THIS INFORMATION REPLACES THE INSERT IN THE PACK

Unlicensed BCG Vaccine (Freeze Dried) supplied by InterVax Ltd, Canada and manufactured by BB NCIPD Ltd, Bulgaria.

ADDITIONAL INSTRUCTIONS FOR USE OF BCG VACCINE SUPPLIED BY INTERVAX LTD AND MANUFACTURED BY BB NCIPD LTD.

Introduction

As colleagues will be used to administering the BCG vaccine supplied by the Statens Serum Institute (SSI), this leaflet provides guidance on use of the InterVax product. Please discard the information leaflet supplied in the box and use this instead.

Public Health England imports BCG Vaccine from BB NCIPD Ltd through InterVax Ltd and arranges for Movianto UK to distribute the product on its behalf.

The product does not have a marketing authorisation (a licence) for use in the UK. Therefore, in accordance with the Human Medicines Regulations 2012, a Patient Group Direction (PGD) **cannot** be used to supply or administer this vaccine. This vaccine will need to be prescribed by using a Patient Specific Direction (PSD), prescription or patient medicines administration chart.

IT IS IMPORTANT TO NOTE THE FOLLOWING

- The presentation in each pack is 20 x 1ml amber glass ampoules of lyophilised powder. A separate pack of 20 x 1ml clear glass ampoules of diluent will also be supplied.
- The BCG vaccine should be reconstituted only with the diluent supplied which is labelled "DILUENT FOR BCG VACCINE (SALINE)". No other diluent should be used.
- The vaccine is to be administered by intradermal injection only.
- Ideally the reconstituted vaccine should be used immediately or within a short period of time. However, if not used immediately, the reconstituted vaccine should be stored away from light, at between 2° and 8°C and must discarded after 6 hours. Care should be taken when storing the reconstituted vaccine to ensure it remains upright.

PLEASE ENSURE THAT ALL STAFF WHO MAY BE INVOLVED IN THE ADMINSTRATION OF BCG VACCINE ARE AWARE OF THIS INFORMATION.

If you require additional information please contact vaccinesupply@phe.gov.uk

Some vaccine ampoules supplied by InterVax have vaccine vial monitors attached. Vaccine vial monitors (VVMs) are separate labels placed on the neck of the ampoules of BCG vaccine supplied through BB-NCIPD Ltd Sofia, Bulgaria.

This is a colour time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of the square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring, or of a darker colour than the ring, then the ampoule should be discarded.

PHE has robust cold chain management arrangements in place up to the point of delivery, therefore absence of the VVM from some batches does not prevent safe use of the vaccine as long as the cold chain has been maintained post-delivery.

✔ **DO USE** if expiry date has not been passed	✘ **DO NOT USE** please discard immediately
	
	

1. Composition

Each ampoule (maximum 10 Adult or 20 Infant doses) contains:

- Active substance: Mycobacterium bovis BCG – 0.5 mg moist weight of BCG which correspond to 0.15 mg dry weight and between 1.5 – 6.0 x 10^6 viable units.
- Stabilizer: Sodium L-glutamate monohydrate – 3.0 mg per ampoule.

Each single adult dose (0.1 ml) contains:

- Active substance: Mycobacterium bovis BCG – 0.05-mg moist weight of BCG that corresponds to between 1.5 – 6.0 x 10^5 viable units.
- Stabilizer: Sodium L-glutamate monohydrate– 0.3 mg per dose.

Each single paediatric dose (0.05ml) contains:

- Active substance: Mycobacterium bovis BCG – 0.025-mg moist weight of BCG that corresponds to between 0.75 – 3.0 x 10^5 viable units.
- Stabilizer: Sodium L-glutamate monohydrate– 0.15 mg per dose.

2. Clinical details

2.1. Recommendations for use

The product is used for the active immunisation against tuberculosis in line with the UK national vaccination programme. This may require pre-vaccination screening using Mantoux (PPD) testing. For advice see: www.gov.uk/government/publications/tuberculosis-the-green-book-chapter-32

Further information for health professionals on the use of Intervax BCG vaccine is available here: www.gov.uk/government/publications/intervax-bcg-vaccine-training-slideset-for-healthcare-professionals

2.2. Dosage

For adults and infants aged 12 months and over a dose of 0.1 ml of the reconstituted vaccine should be injected intradermally.

For Infants under 12 months of age a dose of 0.05 ml of the reconstituted vaccine should be injected intradermally.

Pharmacodynamic properties: Vaccination with BCG Vaccine elicits a cell-mediated immune response that confers protection to infection with M. tuberculosis.

2.3. Method of administration

Reconstitution

Healthcare workers who reconstitute InterVax BCG vaccine should ensure prior to opening the ampoule that their hands are decontaminated using detergent and water or alcohol hand gel. During reconstitution, disposable, non-sterile gloves must be worn.

BCG vaccine from InterVax is sealed under vacuum. The ampoule content is a very light powder and the force of air sucked into the ampoule during opening can blow the content out without notice. Extra attention should be given when opening these ampoules, otherwise the ampoule content can be lost before use.

The ampoule should be gently tapped so that the powdered mass falls to the bottom of the ampoule.

Special care should be taken when opening the ampoules and the square of plastic provided with the pack, should be used to wrap around the ampoule, after which the neck can be broken off carefully to avoid escape of the dry powder. Each pack of 20 ampoules is routinely supplied with one plastic square. This should be retained for use in opening the 20 ampoules of freeze dried powder.

As a temporary measure, each pack of 20 ampoules of InterVax BCG will be supplied with additional plastic squares as a safeguard, to cover inadvertent disposal of the supplied single sheet. This temporary measure is in place to enable staff to become accustomed to using and preparing this vaccine. These additional squares should be retained if unused as future vaccine supplies are unlikely to come with additional plastic squares.

In the event that you do not have a plastic square to aid the safe opening of the ampoule containing the freeze dried BCG powder, do NOT attempt to open it without a protective film. An alternative to the plastic square should be used, for example a film such as Parafilm (available via NHS Supply Chain) or any other similar product can used. If you injure your hand while doing this, discard the ampoule because the content may have become contaminated. Cover the wound before opening a new ampoule.

The ampoule should then be visually inspected to ensure the powder is present before reconstitution.

Draw up the entire content of the diluent ampoule supplied by InterVax into a syringe using a long needle. Reconstitute the vaccine by slowly and very gently adding the entire content of the syringe containing the diluent to the freeze dried powder. In order to prevent aerosolisation of the powder, the diluent is best added by angling the ampoule containing the freeze dried powder slightly, so that the diluent slowly trickles down the inside of the glass, into the powder. Once all the diluent has been added to the powder, mix by slowly drawing up and down in the syringe several times. Discard the mixing syringe and needle safely and use a new one for the immunisation.

Two to three minutes later a homogeneous slightly opalescent colourless suspension appears. The reconstituted vaccine should be inspected visually for any foreign particulate matter prior to administration. If observed, the vaccine must be discarded.

Care should be taken when storing the reconstituted vaccine to ensure it remains upright.

After removing and safe disposal of gloves, hands should be washed using detergent and water (not alcohol hand gel).

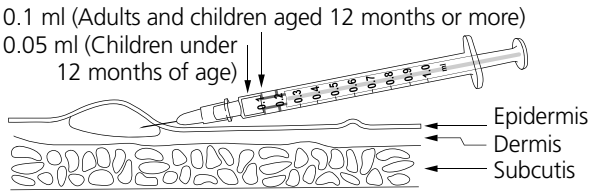
As an added precaution, it is recommended that healthcare workers who are severely immunocompromised, should not reconstitute or administer InterVax BCG vaccine (note this advice is specific to InterVax BCG only and not other live vaccines). For details of immunocompromise, see pages 43 to 45 in the following link: www.gov.uk/government/uploads/system/uploads/attachment_data/file/147824/Green-Book-Chapter-6-v2_0.pdf

Administration
For intradermal injection only.

The injection site should be clean and dry, but not cleaned with an antiseptic. The use of a special tuberculin syringe and sterile 26-gauge 10mm (0.45mm × 10mm) short bevelled needle is recommended for each injection. Other needles are not suitable and should not be used. The needle should be primed before administering the intradermal injection. Jet injectors or multiple puncture devices should not be used to administer the vaccine.

InterVax BCG vaccine should be injected strictly by intradermal injection in the arm, over the distal insertion of the deltoid muscle onto the humerus (approx. one third down the upper left arm).

The needle should be introduced with its aperture upwards and the injection is given slowly.



The usual reaction to successful BCG vaccination is induration at the injection site, followed by a local lesion which starts as a papule two or more weeks after vaccination. It may ulcerate and then slowly subside over several weeks or months to heal, leaving a small, flat scar. It may also include enlargement of a regional lymph node to less than 1 cm.

The injection site is best left uncovered to facilitate healing.

Further training materials on administration of the InterVax BCG vaccine are available at www.gov.uk/government/publications/intervax-bcg-vaccine-training-slideset-for-healthcare-professionals

2.4. BCG vaccine should not be administered to the following groups

The vaccine should not be given to:
- those who have already had a BCG vaccination
- those with a past history of TB
- those with an induration of 5mm or more following Mantoux (SSI) tuberculin skin testing
- those who have had a confirmed anaphylactic reaction to a component of the vaccine
- neonates in a household where an active TB case is suspected or confirmed
- people who are immunocompromised by virtue of disease or treatment, e.g.:
  - patients receiving corticosteroid or other immunosuppressive treatment, including general radiation. Inhaled steroids are not a contraindication,
  - this also includes infants exposed to TNF-α antagonists or other immunomodulating biological medicines in utero or via breastfeeding, for as long as a postnatal influence of the immune status of the infant remains possible (at least until the infant is aged 6 months). If there is any doubt as to whether an infant due to receive a live attenuated vaccine may be immunosuppressed due to the mother's therapy, including exposure through breast-feeding, specialist advice should be sought.
  - those suffering from a malignant condition such as lymphoma, leukaemia, Hodgkin's disease or other tumour of the reticuloendothelial system.

BCG is contraindicated in symptomatic HIV-positive individuals. In countries such as the UK where the risk of TB is low, it is recommended that BCG is also withheld from all those known to be or suspected to be HIV positive, regardless of clinical status. Where vaccination is indicated, for example infants born to HIV-positive mothers, this can be administered after two appropriately timed negative postnatal PCR tests for HIV infection.

BCG Vaccine should not be administered to individuals known to be hypersensitive to any component of the vaccine, listed in section 3.

BCG Vaccine should not be given to patients who are receiving, or previously received anti-tuberculosis drugs.

2.5. Additional precautions

Minor illnesses without fever or systemic upset are not valid reasons to postpone immunisation. If an individual is acutely unwell, immunisation should be postponed until they have fully recovered. This is to avoid confusing the differential diagnosis of any acute illness by wrongly attributing any sign or symptoms to the adverse effects of the vaccine.

Individuals with generalised septic skin conditions should not be vaccinated. If eczema exists, an immunisation site should be chosen that is free from skin lesions.

BCG Vaccine should not be administered intravascularly in any circumstances.

Pregnancy
BCG vaccination should not be given during pregnancy. Even though no harmful effects of BCG vaccination on the fetus have been observed, further studies are needed to prove its safety.

Breastfeeding
Breast-feeding is not a contraindication to BCG. As above, if there is any doubt as to whether an infant due to receive BCG vaccine may be immunosuppressed due to the mother's therapy, including exposure through breast-feeding, specialist advice should be sought.

2.6. Possible interaction with other medicinal products

To ensure timely protection InterVax BCG can be given at the same time or at any time before or after other vaccines such as DTaP/IPV+Hib and hepatitis B vaccines.

BCG can be administered at the same time as other live vaccines including rotavirus, live attenuated influenza vaccine (LAIV), oral typhoid vaccine, yellow fever, varicella, zoster and MMR. Other vaccines to be given at the same time as InterVax BCG vaccine should not be given into the same arm. 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.

For further information, see this link: www.gov.uk/government/publications/revised-recommendations-for-administering-more-than-1-live-vaccine

2.7. Possible side effects

The expected reaction to successful vaccination with BCG Vaccine includes a papule at the injection site. This is followed after two or three weeks by a red nodule. In some cases a small abscess is formed which later develops into a small ulcer. This heals without treatment in a few weeks.

Enlargement of the axillary lymph-nodes may occasionally develop after vaccination but spontaneous resolution usually occurs after a few months. In rare cases perforation and persistent suppuration can accompany the lymph-node enlargement and anti-tuberculosis treatment may be indicated.

Keloid and lupoid reactions may also occur at the site of injection.

Severe injection site reactions, large, local discharging ulcers, abscesses and keloid scarring are most commonly caused by faulty injection technique, excessive dosage or vaccinating individuals who are tuberculin positive.

Other adverse reactions to the vaccine include headache and fever.

Allergic reactions (including anaphylactic reactions), more severe local reactions such as abscess formation, and disseminated BCG complications (such as osteitis or osteomyelitis) are rare.

2.8. Reporting of suspected side effects

Suspected adverse reactions should be recorded and reported through the Yellow Card Scheme at: yellowcard.mhra.gov.uk

2.9. Overdose

Overdose increases the risk of a severe local reaction and suppurative lymphadenitis, and may lead to excessive scar formation.

Any incident resulting in administration of an overdose of BCG vaccine should be documented according to local policy. The vaccine recipient or their carer and the local chest physician should be informed. The clinician should decide whether preventive chemotherapy is indicated and ensure arrangements are made for appropriate monitoring for early signs of an adverse reaction.

Public Health England

Further supplies can be obtained via:
www.immform.dh.gov.uk

3215089 4p 13K Apr 2018 (APS)

This leaflet was last revised on 04/2018

3. Pharmaceutical form

3.1. List of excipients

Per 0.1ml dose:

Powder:
- Sodium L-glutamate monohydrate (stabilizer) – 0.3 mg per dose

Diluent:
- Sodium chloride – 0.9 mg
- Water for injection – 0.1 ml

3.2. Incompatibilities

BCG Vaccine should not be mixed with other medicinal products.

3.3. Shelf life

36 months from manufacture, (please see labelled expiry date).

When withdrawals are made from the ampoule, the vaccine should only be exposed to the light for the minimum amount of time. Ideally the reconstituted vaccine should be used immediately or within a short period of time. However, in these current exceptional circumstances, it is important to manage the shortage of BCG and maintain the vaccination programme. If it is not possible to use the contents of the ampoule immediately then the open ampoule can be stored away from light between 2°C and 8°C and used for a maximum period of 6 hours. Care should be taken when storing the reconstituted vaccine to ensure it remains upright.

3.4. Storage instructions

Store in original container.

Keep at a temperature of between +2°C and +8°C and protect from light.

DO NOT FREEZE. If the product is frozen please contact vaccinesupply@phe.gov.uk for advice.

This vaccine should be kept out of the reach and sight of children.

3.5. Nature and contents of container

BCG is freeze-dried preparation in ampoules containing a maximum of 10 adult (or 20 infant) doses, sealed under vacuum. The final packing is a box with two blister-type carriers, each of which contains 10 ampoules of BCG vaccine. The diluent is in ampoules, containing 1 ml Sodium Chloride 9 mg/ml. The final packing of diluent is also a box with two blister-type carriers, each of which contains 10 ampoules.

Supplier

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