Package leaflet: Information for the user

BCG-medac, powder and solvent for intravesical suspension

Bacillus Calmette-Guérin

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What BCG-medac is and what it is used for

The full name of this medicine is BCG-medac, powder and solvent for intravesical suspension. It will be referred to as BCG-medac in the rest of this leaflet.

BCG-medac contains weakened (attenuated) *Mycobacterium bovis* bacteria with low infectious potential.

BCG-medac stimulates the immune system and is used to treat several types of cancer in the urinary bladder. It is effective if the cancer is limited to the cells lining the inside of the bladder (urothelium) and has not invaded the inner tissues of the bladder.
BCG-medac is administered directly into the bladder by instillation.

For the flat lesion form of bladder cancer (carcinoma *in situ*) BCG-medac is used to cure the disease confined to the bladder lining. There are different grades of cancer that can affect the lining of the bladder and the layer of cells next to the lining (lamina propria).

BCG-medac is also used to prevent the cancer coming back (prophylactic treatment).

2. What you need to know before you use BCG-medac

Do not use BCG-medac
- if you are allergic to viable BCG (Bacillus Calmette-Guérin) bacteria or any of the other ingredients of this medicine (listed in section 6.).
- if the activity of your immune system is reduced or you suffer from immune deficiencies, whether due to simultaneous disease (e.g. positive HIV serology, leukaemia, lymphoma), cancer therapy (e.g. cytostatic medicines, radiation) or immunosuppressive therapy (e.g. corticosteroids).
- if you are suffering from active tuberculosis.
- if your bladder or adjacent regions have been treated by radiotherapy before.
- if you are breast-feeding.

- if you have had surgery through the urethra (TUR; transurethral resection), a sample of your bladder tissue (bladder biopsy) was taken or you suffered injury by catheter (traumatic catheterisation) during the previous 2 – 3 weeks.
- if you have bladder perforation.
- if there is visible blood in your urine (macrohaematuria).
- if you suffer from an acute infection of the urinary tract.

BCG-medac must not be used for administration under or into the skin, into the muscle or vein or for vaccination. It must be administered directly into the bladder by instillation.

Warnings and precautions

Your doctor hands over to you a patient alert card, which you should always carry with you (see also section 4).

Talk to your doctor or pharmacist before using BCG-medac
- if you have a fever or presence of blood in the urine. Then, treatment with BCG-medac should be postponed.
- if you have a low bladder capacity as it may decrease even more after the treatment.
- if you are HLA-B27 (human leukocyte antigen B27) positive as you could have an increase of the occurrence of inflammation of the joints (reactional arthritis).
- if you have arthritis with inflammation of the skin, eyes, and the urinary tract (Reiter's syndrome).
- if you have a localised dilatation of a blood vessel (aneurysm) or prosthesis. You may get an infection of implants or grafts.
- if you have liver problems or take drugs which may affect the liver. This is particularly important if triple antibiotic therapy with so-called anti-tuberculosis drugs is considered.

General hygiene
After instillation sit down before urinating to prevent sprinkling of the urine and to avoid contamination of the area with BCG-bacteria.
It is recommended to wash your hands and genital area after urinating. This applies especially to the first urination following BCG-treatment. If skin lesions are contaminated, an appropriate disinfectant should be used (ask your doctor or pharmacist).

Detection of Bacillus Calmette-Guérin
The detection of BCG-bacteria is generally difficult. A negative test result does not rule out an infection with BCG outside the bladder.

Urinary tract infection
Your doctor should determine that you do not have an acute urinary tract infection before each bladder treatment with BCG. If an acute urinary tract infection is diagnosed during BCG-therapy, treatment should be interrupted until the urinalysis is normalised and therapy with antibiotics is completed.

Patients with contact to immunosuppressed persons
If you are treated with BCG-medac you must comply with general hygienic standards as stated above. This is of utmost importance if you are in contact with immunosuppressed persons, as BCG-bacteria can be harmful to patients with a weak immune system. However, a man-to-man transmission of the bacteria has not been reported yet.

Sexual transmission
You should use a condom during sexual intercourse for one week after BCG-therapy to be sure that no sexual transmission of BCG-bacteria happens.

Other medicines and BCG-medac
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

This is especially important with the following medicines, as BCG-bacteria are sensitive to:
- antituberculous agents (e.g. ethambutol, streptomycin, p-aminosalicylic acid (PAS), isoniazid (INH) and rifampicin);
- antibiotics (fluoroquinolones, doxycycline or gentamicin);
- antiseptics;
- lubricants.

BCG-bacteria are resistant to pyrazinamide and cycloserine.

Pregnancy, breast-feeding and fertility

Pregnancy

You should not use BCG-medac if you are pregnant or you think you might be pregnant.

Breast-feeding

Do not take BCG-medac when you are breast-feeding.

Fertility
BCG was found to adversely affect the production of sperm and might cause low concentration or absence of sperm in semen. This effect was reversible in animals. However, men should seek advice about the possibility of sperm preservation before starting therapy.

Driving and using machines
This medicine could have an effect on your ability to drive or operate machines. Do not drive or operate machinery until you know what effect BCG-medac has on you.

Talk to your doctor, nurse or pharmacist if you are unsure about anything.

3. How to use BCG-medac

Dosage
BCG-medac is prepared and administered by experienced healthcare professionals only. The content of one vial is required for one bladder treatment.

Administration
BCG-medac is introduced into the bladder at low pressure by means of a catheter.
The medicine should remain in the bladder for a period of 2 hours. To allow this, you should not drink over a period of 4 hours before the treatment and for 2 hours after the treatment.

While the suspension remains in your bladder it should have sufficient contact with the entire mucosal surface, moving around supports the treatment. After 2 hours you should empty your bladder in a sitting position to avoid spillage.

Unless you are on a restricted fluid regimen, you are advised to drink abundantly for 48 hours after each treatment.

Use in children
Safety and efficacy in children have not been established for BCG-medac.

Use in the elderly
There are no special instructions for the use in the elderly. However, liver function should be considered before BCG is administered.

Duration of treatment
As a standard treatment schedule (induction therapy) you will receive one intravesical treatment with BCG-medac per week for 6 consecutive weeks. After a period of 4 weeks without treatment you may receive an additional intravesical administration called maintenance therapy for at least one year as described below. Your doctor will talk to you about this.

Induction therapy
- BCG-therapy should begin about 2 – 3 weeks after surgery through the urethra (TUR; transurethral resection) or taking of a bladder tissue sample (bladder biopsy) and without injury by catheter (traumatic catheterisation). It will be repeated at weekly intervals for 6 weeks.
- After this many people get maintenance therapy, where you may be given more doses.

Maintenance therapy
- Maintenance therapy consists of 3 treatments at weekly intervals given for a minimum of 1 year up to 3 years, at month 3, 6, 12, 18, 24, 30, and 36. With this scheme you will receive a total of 15 to 27 treatments during a period of 1 to 3 years.

Your doctor will discuss with you the need for maintenance therapy every 6 months beyond the first year of treatment, if necessary.

Although maintenance therapy reduces the possibility of the cancer coming back and may reduce its ability to progress, the side effects and discomfort of the treatment may outweigh the benefits for some patients. Thus, it is important that your doctor discusses the draw-backs of the treatment and your own preferences with you before beginning or continuing maintenance treatment.

If you use more BCG-medac than you should
Overdose is unlikely to occur as one vial of BCG-medac corresponds to one dose instilled into the bladder. There are no data indicating that an overdose may lead to any other symptoms than the described side effects (see section 4).

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
The side effects of BCG-treatment are frequent but generally mild and temporary. Adverse reactions usually increase with the number of BCG-treatments.

However, the most serious side effect is a severe systemic infection. Tell your doctor immediately if you experience the following symptoms which can occur at any time and are sometimes delayed, and may develop weeks, months or even years after your last dose.
Show your patient alert card to your treating physicians.

- Fever above 39.5 °C during at least 12 hours or fever above 38 °C lasting for weeks; night sweats
- Weight loss of unknown origin
- Feeling increasingly poorly
- Signs of inflammation may differ and present as

    - breathing difficulties or a cough that do not feel like a normal cold (miliary pneumonia)
    - liver problems: a feeling of pressure in right upper abdomen or, liver function test abnormalities (especially an enzyme called alkaline phosphatase), or
    - pain and redness of the eye, vision problems or blurry vision; “pink eye”
- A so-called granulomatous inflammation which has been shown in a biopsy.

Systemic BCG-infection/reaction
If the bladder is accidentally injured during treatment with BCG medac or BCG medac is administered into a muscle or vein this can result in a severe general infection with BCG. Severe systemic BCG-infection can lead to BCG-sepsis. BCG-sepsis is a life-threatening situation. Talk immediately to your physician if you experience a symptom or sign that worries you or contact a physician specialised in infectious diseases! However, the infection is not virulent. Your doctor will prescribe you medicine for your side effects and BCG-treatment may be interrupted.

In contrast to a BCG-infection, a BCG-reaction often presents with low-grade fever, flu-like symptoms and general discomfort for 24 – 48 hours as a starting immune reaction. You doctor may prescribe some medicine to treat the symptoms. Talk to your doctor, if the symptoms worsen.

Delayed BCG-infection
In single cases BCG-bacteria may remain in the body for years. This infection might present at any time and sometimes the symptoms and signs of an infection occur lately, even years after the last dose of BCG medac has been administered. Signs of inflammation could be similar to a severe BCG-infection/reaction like mentioned above. Problems with your implant or graft may also be a side effect of BCG-treatment and require urgent treatment.
Therefore, it is of utmost importance to take your personal alert card with you and hand it over to every doctor treating you to ensure appropriate treatment in case of an occurrence of a delayed BCG-infection. The doctor will also be able to assess if the symptoms are a side effect of your BCG-therapy or not.

In the following, please find a complete list of side effects that may occur:

Very common: may affect more than 1 in 10 people
- Feeling sick (nausea)
- Bladder inflammation (cystitis), inflammatory reactions (granulomata) of the bladder. These side effects may be an essential part of the anti-tumour activity.
- Frequent urination with discomfort and pain. This may affect up to 90 % of the patients.
- Inflammatory reactions of the prostate gland (asymptomatic granulomatous prostatitis)
- Temporary systemic BCG-reactions such as fever below 38.5 °C, flu-like symptoms (malaise, fever, chills) and general discomfort
- Fatigue

Common: may affect up to 1 in 10 people
- Fever higher than 38.5 °C
- Muscle pain (myalgia)
- Diarrhoea
- Abdominal pain
- Incontinence

Uncommon: may affect up to 1 in 100 people
- Severe systemic BCG-reaction/infection, BCG-sepsis (see below for more detailed information)
- Deficiency of cells in the blood (cytopenia)
- Anaemia (decrease in haemoglobin in the blood)
- Reiter’s syndrome (arthritis with inflammation of the skin, eyes, and the urinary tract)

- Inflammation of the lungs (miliary pneumonitis)
- Inflammatory reactions of the lung (pulmonary granuloma)
- Inflammation of the liver (hepatitis)
- Skin abscess
- Skin rash, joint inflammation (arthritis), joint pain (arthralgia). In most cases, these side effects are signs of an allergic (hypersensitivity) reaction to BCG. In some cases it may be necessary to discontinue treatment.
- Urinary tract infection, presence of blood in the urine (macroscopic haematuria)
- Abnormally small bladder (bladder retraction), abnormally low urine flow (urinary obstruction), bladder contracture
- Inflammation of the testes (orchitis)
- Inflammation of the epididymis (epididymitis)
- Inflammatory reaction of the prostate gland (symptomatic granulomatous prostatitis)
- Low blood pressure (hypotension)
- Abnormal liver function test

Rare: may affect up to 1 in 1,000 people
- Vascular infection (e.g. infected localised dilatation of a blood vessel)
- Kidney abscess

Very rare: may affect up to 1 in 10,000 people
- BCG-infection of implants and surrounding tissue (e.g. aortic graft infection, cardiac defibrillator, hip or knee arthroplasty)
- Inflammation of the lymph nodes of the neck (cervical lymphadenitis), regional lymph node infection
- Allergic (hypersensitivity) reaction (e.g. oedema of eyelids, cough)
- Inner eye inflammation (chorioretinitis)
- Conjunctivitis (“pinkeye”), uveitis (inflammation of the uvea of the eye)
- Vascular fistula
- Vomiting, intestinal fistula, inflammation of the peritoneum (peritonitis)
- Infection of bone and bone marrow by bacteria (osteomyelitis)
- Bone marrow infection
- Psoas abscess (abscess of the muscle of the loin)
- Inflammation of the testes (orchitis) or epididymis (epididymitis) resistant to antituberculous therapy
- Infection of the glans penis
- Swelling in your arms or legs

Not known: frequency cannot be estimated from the available data
- Inflammation of the blood vessels (possibly in the brain)
- Genital disorders (e.g. vaginal pain)
- Painful sexual intercourse (dyspareunia)
- Severe immunologic reaction with fever, enlarged liver, spleen and lymph nodes, jaundice and rash (haemophagocytic syndrome)
- Renal failure, inflammation of the kidney tissue, chambers, pelvis (pyelonephritis, nephritis [including tubulointerstitial nephritis, interstitial nephritis and glomerulonephritis])
- Absence or low level of sperm in semen (azoospermia, oligospermia)
- Elevation of Prostatic specific antigen (PSA, a prostate laboratory test)

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store BCG-medac

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and carton after EXP.

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.

Store in the original package in order to protect from light.

The physical and chemical in-use stability has been demonstrated for 24 hours when stored protected from light at room temperature (20 °C – 25 °C) or refrigerator temperature (2 °C – 8 °C).
From a microbiological point of view, the medicinal product should be used immediately.
If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C, unless reconstitution has taken place in controlled and validated aseptic conditions.

6. Contents of the pack and other information

What BCG-medac contains
The active ingredient is viable BCG (Bacillus Calmette-Guérin) bacteria (seed RIVM derived from seed 1173-P2).

After reconstitution one vial contains:
BCG-seed RIVM derived from seed 1173-P2
2×10^8 to 3×10^9 viable units

The other ingredients of the powder are: polygeline, glucose anhydrous and polysorbate 80.
The other ingredients of the solvent are: sodium chloride and water for injections.

What BCG-medac looks like and contents of the pack
BCG-medac consists of a white or almost white powder or porous cake with shades of yellow and grey and a colourless, clear solution used as solvent. There are packages of 1 or 3 or 5 or 6 vials with or without catheter(s) and Luer-Lock to conical connector(s). Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

medac
Gesellschaft für
klinische Spezialpräparate mbH
Theaterstr. 6
22880 Wedel
Germany

This leaflet was last revised in 12/2024.

The following information is intended for healthcare professionals only:

Treatment of symptoms, signs and syndrome

Symptoms, signs or syndrome	Treatment
1. Symptoms of vesical irritation lasting less than 48 hours	Symptomatic treatment.
2. Symptom of vesical irritation lasting more or equal to 48 hours	Discontinue therapy with BCG-medac and start treatment with quinolones. If after 10 days no complete resolution is observed, administer isoniazid (INH)* for 3 months. In case of antituberculous treatment, therapy with BCG-medac should definitively be discontinued.
3. Concomitant bacterial infection of urinary tract	Postpone BCG-medac therapy until the urinalysis is normalised and treatment with antibiotics is completed.
4. Other genitourinary undesirable effects: symptomatic granulomatous prostatitis, epididymitis and orchitis, urethral obstruction and renal abscess	Discontinue therapy with BCG-medac. Consider a consultation with a specialist for infectious diseases. Administer isoniazid (INH)* and rifampicin*, for 3 to 6 months according to severity. In case of antituberculous treatment, therapy with BCG-medac should definitively be discontinued.
5. Fever less than 38.5 °C lasting less than 48 hours	Symptomatic treatment with paracetamol.
6. Cutaneous eruption, arthralgias or arthritis or Reiter`s syndrome	Discontinue therapy with BCG-medac. Consider a consultation with a specialist for infectious diseases. Administer antihistaminic or non-steroidal anti-inflammatory drugs. Cortisone therapy should be considered in case of an immune-mediated reaction. If no response, administer isoniazid* for 3 months. In case of antituberculous treatment, therapy with BCG-medac should definitively be discontinued.
7. Systemic BCG-reaction/infection** without septic shock signs	Definitely discontinue treatment with BCG-medac. Consider a consultation with a specialist for infectious diseases. Administer a triple drug antituberculous therapy* for 6 months and low dose corticosteroid therapy.
8. Systemic BCG-reaction/infection with septic shock signs	Definitely discontinue treatment with BCG-medac. Administer immediately a triple antituberculous therapy* combined with high-dose, quick-acting corticosteroids. Seek the opinion of a specialist for infectious diseases.

***Caution**: BCG-bacteria are sensitive to all antituberculous medicinal products currently used, except for pyrazinamide. If a triple antituberculous therapy is necessary, the combination usually recommended is isoniazid (INH), rifampicin and ethambutol.
** definition see above

Important information on the use of BCG-medac
BCG-medac may only be used by experienced healthcare professionals.
Ensure suitable storage (see section 5) and the integrity of the packaging.
BCG-medac should be administered in the conditions required for intravesical endoscopy.

BCG-medac must not be administered subcutaneously, intradermally, intramuscularly, intravenously or for vaccination against tuberculosis.
The Luer-Lock catheter connector of the solvent bag may only be used for intravesical instillation!

Basic principles and protective measures for the use of BCG-medac
In general, direct contact with BCG-medac should be avoided. BCG-medac is a medicinal product that can cause infection in humans and pose a risk to healthcare professionals. A hazard may occur if the medicinal product is able to enter the body via injured skin, if aerosols are inhaled, droplets get into

the eyes or come into contact with mucous membranes, or if ingested. Do not eat, drink or smoke in the work areas and do not store any food, drinks or tobacco products here. BCG-medac must not be handled in a room in which cytotoxic medicinal products are being prepared for intravenous use, nor handled by personnel who are preparing cytotoxic medicinal products for intravenous use.
The medicinal product must not be handled by persons with a known immunodeficiency.
It is recommended that closed, splashproof protective gown, disposable gloves, an FFP2 respirator mask and safety goggles with side shields are worn as personal protective equipment during handling.
BCG-medac may only be transported in closed containers (for storage conditions after reconstitution, see section 5).
After finishing work, wipe down the work surfaces with suitable disinfectant solution. After working and in the case of contact with skin, disinfect your hands using hand disinfectant, allow them to dry, wash them and use skin care products.

Tuberculin cutaneous tests
The intravesical treatment with BCG-medac could induce sensitivity to tuberculin and complicate subsequent interpretation of tuberculin cutaneous tests for mycobacterial infection diagnosis. Therefore, reactivity to tuberculin should be measured before administration of BCG-medac.

Preparation of the reconstituted intravesical suspension
Before use, the medicinal product must be resuspended under aseptic conditions using sterile 0.9% (9 mg/mL) sodium chloride solution (see instructions for use, step 7). The catheter should be placed with special care to avoid injuries to the urethral and urinary bladder epithelium, which can lead to systemic BCG infection. Use of a lubricant is recommended to minimise the risk of traumatic catheterisation and to make the procedure more comfortable. Women might need less lubricant than men. It has not been observed that a possible antiseptic effect of the lubricant may influence the efficacy of the product. Drain the bladder after catheterisation to reduce the amount of lubricant potentially introduced before you administer BCG-medac. The suspension is mixed by gently swirling before use. Macroscopically visible particles have no influence on the efficacy and safety of the medicinal product.
The contents of the vial are intended for single use/single dose only. Any remaining suspension must be disposed of.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Behaviour in the event of emergencies and spillage of BCG-medac
Wear protective clothing and avoid stirring up dust.
Cover the spilled BCG-medac suspension with cellulose and moisten it with a disinfectant that is proven to be effective against mycobacteria. After wiping up the spilled BCG-medac suspension, clean the surface again with disinfectant solution and allow it to dry. Spillage on the skin should be treated using a suitable disinfectant.

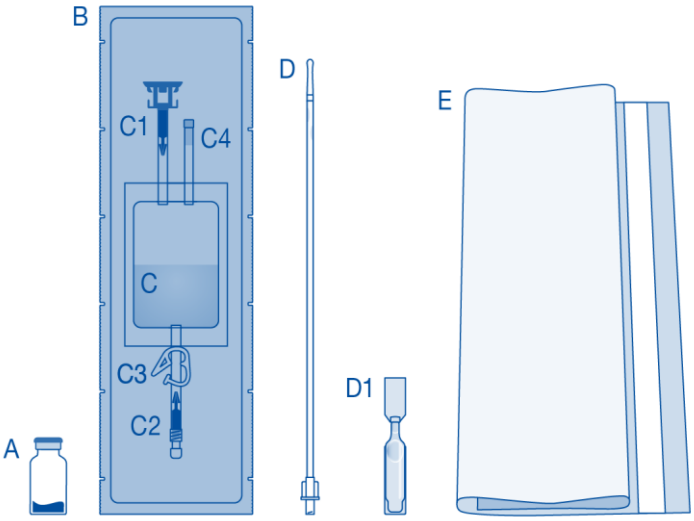
First aid
Always consult a doctor in case of contamination.
In case of contact with the skin: remove contaminated clothing. Disinfect and clean the skin and check for contamination of wounds.
In case of contact with the eyes: rinse the affected eye with sufficient eyewash solution or, alternatively, with water. Remove contact lenses if applicable.
In case of ingestion: rinse mouth with plenty of water.
In case of inhalation: ensure a sufficient supply of fresh air.

For further information regarding the catheter please see the corresponding instructions for use.

Instructions for users of BCG-medac

Constituents and application of the instillation set |<with catheter, without Luer-Lock to conical connector>

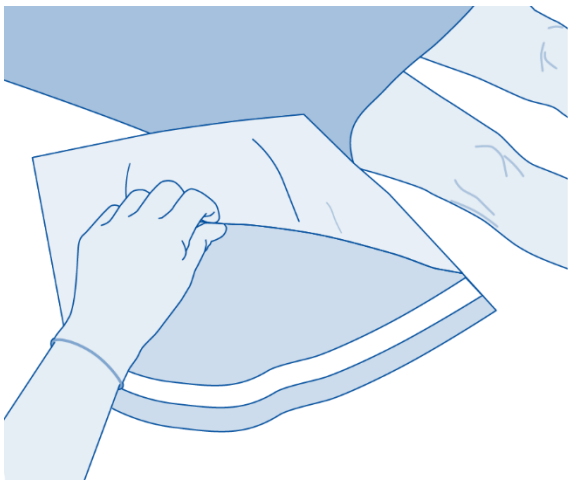
Main constituents of the instillation set



Main constituent	Description
A	Vial with powder
B	Protective cover
C	Solvent bag with 0.9% (9 mg/mL) sodium chloride solution
C1	Vial connector with protective cap and break-open seal
C2	Luer-Lock catheter connector with protective cap and break-open seal
C3	Pressure clamp
C4	Filling port without application function
D	Luer-Lock catheter
D1	Lubricant
E	Disposal bag

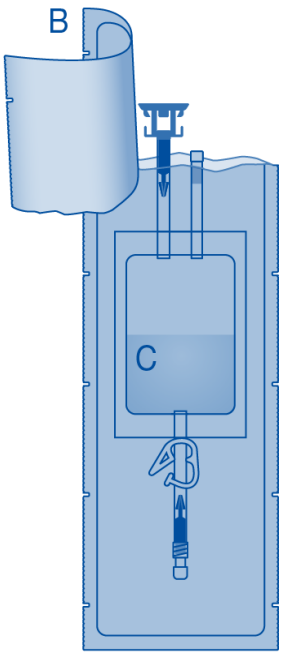
Connecting the vial to the solvent bag

1. Lay out the disposal bag (E) ready for direct disposal of the set after instillation to prevent contamination.

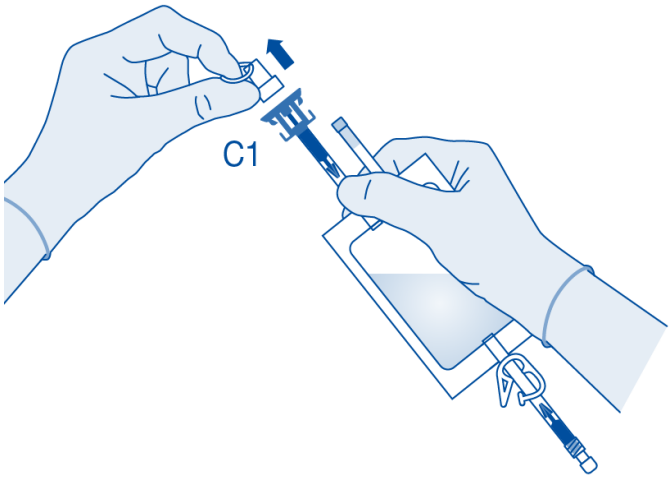


2. Remove the flip-off cap from the vial (A) and disinfect the stopper according to local regulations.

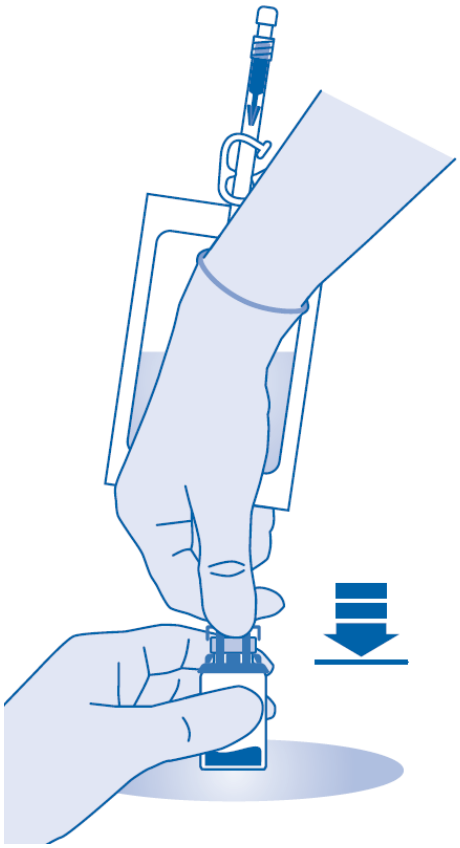
3. Tear open the protective cover (B) of the solvent bag (C) and remove the protective cover completely.



4. Remove the protective cap from the vial connector (C1).

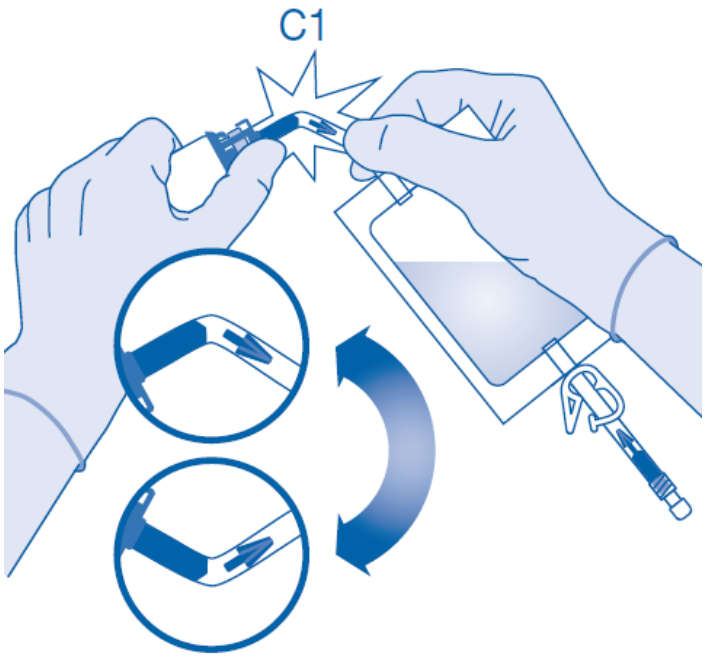


5. Push the connector onto the vial up to the stop.



Mixing the powder with the solvent

6. Bend the break-open seal inside the tube of the vial connector (C1) up and down multiple times to break the seal.



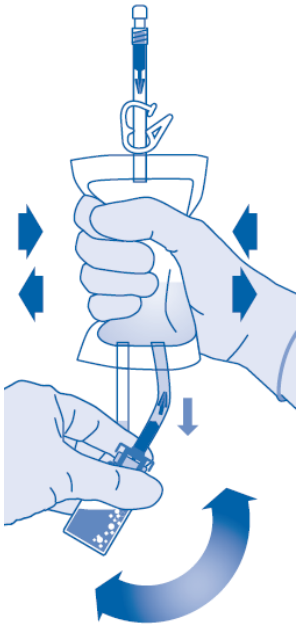
7. Hold the **solvent bag** so that the **vial is below it**.

   Squeeze the solvent bag multiple times to transfer enough solvent into the vial.

   Make sure that the vial is **not** filled completely to allow for the subsequent transfer of the suspension into the solvent bag. Some solvent may remain inside the bag.

   Swirl the vial **slowly** to minimise heavy foaming while mixing the medicinal product with the solvent. If there is a lot of foam, leave the vial to rest briefly (a few minutes).

   The contents of the vial have to form a homogeneous suspension. This may take a few minutes.



8. Turn the **solvent bag** upside down and hold it so that the **vial is above** it.

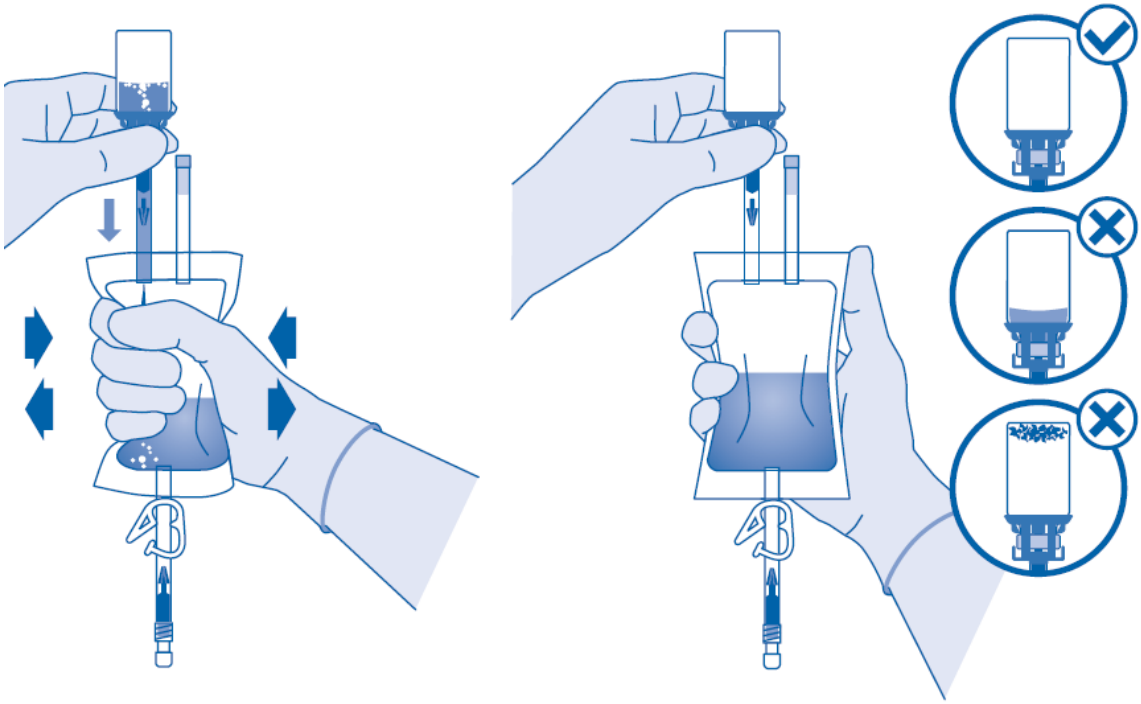
   Hold the vial.

   Squeeze the solvent bag multiple times until the vial is completely empty.

   If any powder remains inside the vial, repeat steps 7 and 8.

   From a microbiological point of view the medicinal product should be used immediately. If the medicinal product is not used immediately, please see section 5 “How to store BCG-medac”.

   The suspension should not be instilled at refrigerator temperature in order to prevent the patient from feeling the need to urinate resulting in a shortened exposure time.



Catheterisation

9. Catheterise the patient according to local regulations and the instructions for use using the enclosed Luer-Lock catheter (D) and lubricant (D1) or another suitable catheter and/or lubricant.

   Empty the urinary bladder using the catheter.

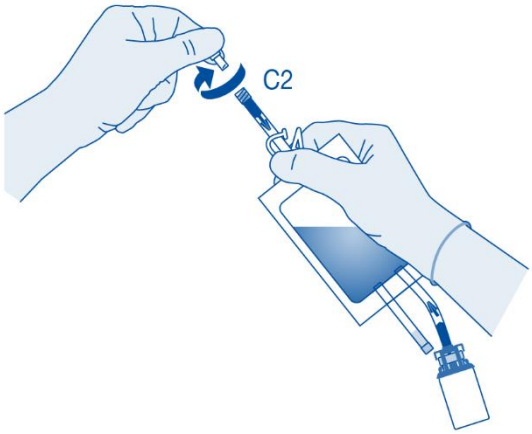
Connecting the catheter to the solvent bag

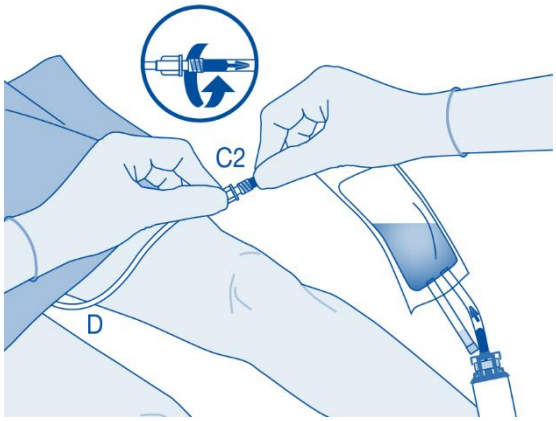
10. To mix any sediments, rotate and swirl the bag before connecting it.

    Do not administer the suspension at refrigerator temperature.

    Remove the protective cap from the catheter connector (C2).

    Connect the patient’s Luer-Lock catheter (D) with the catheter connector (C2) of the solvent bag.

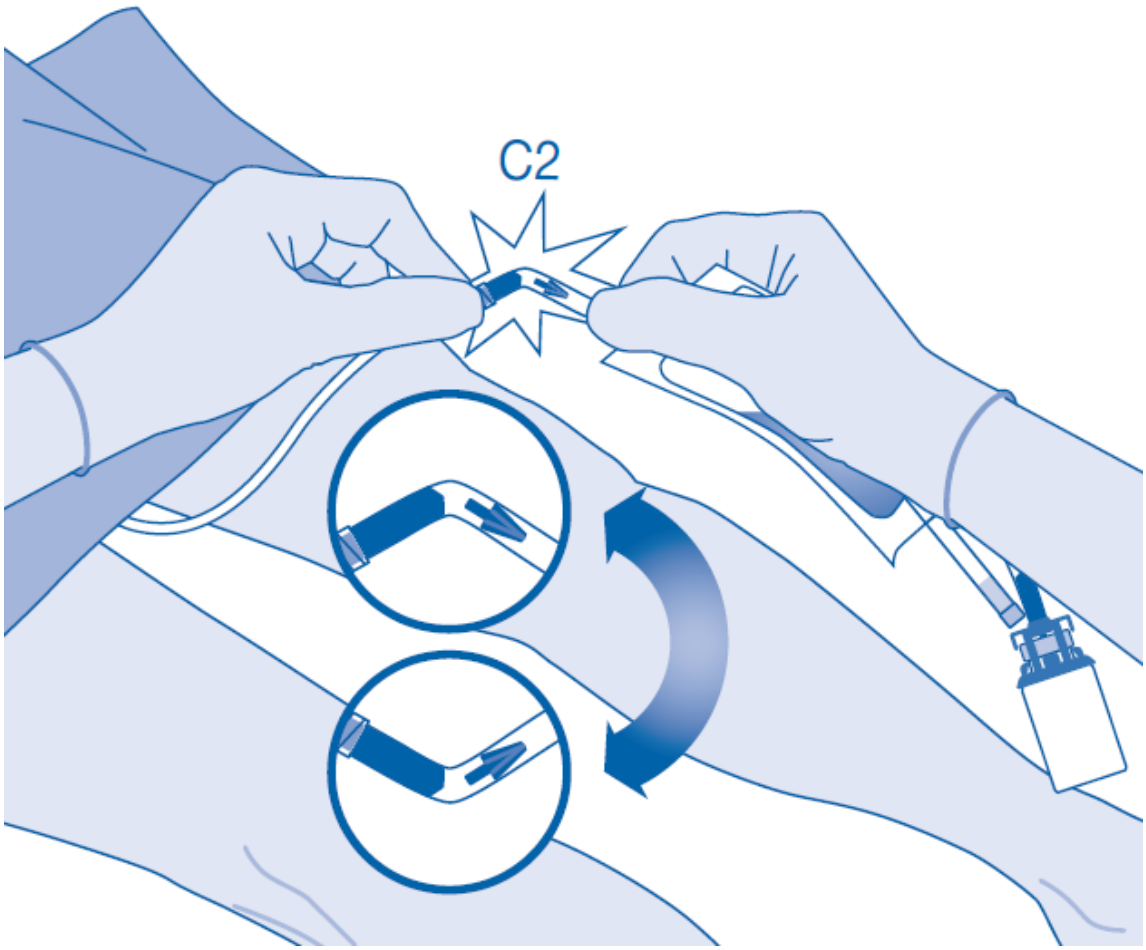




Instillation

11. Bend the break-open seal inside the tube of the catheter connector (C2) up and down multiple times to break the seal.

    Hold the patient's catheter steady while doing so.

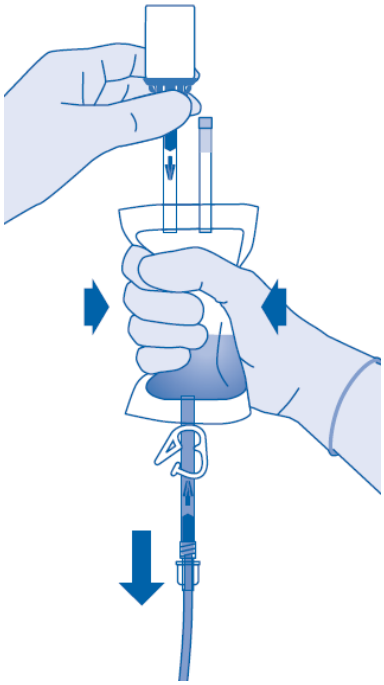


12. Hold the **solvent bag** with the **vial upside down above the bag**.

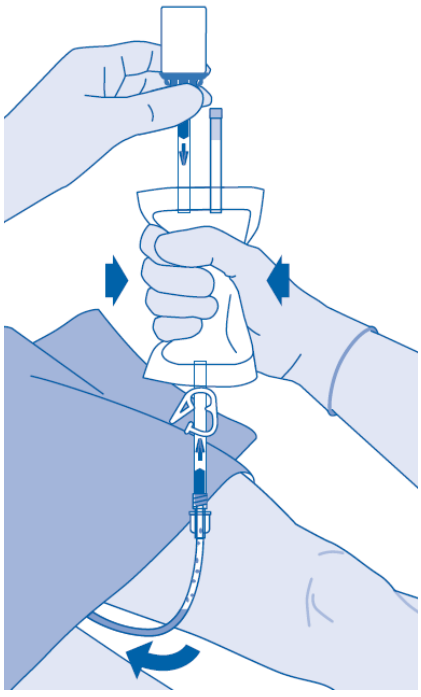
    Squeeze the solvent bag **gently** with the other hand so that the medicinal product is **slowly**

instilled into the patient's urinary bladder.

Continue to squeeze until the solvent bag and the vial are empty.



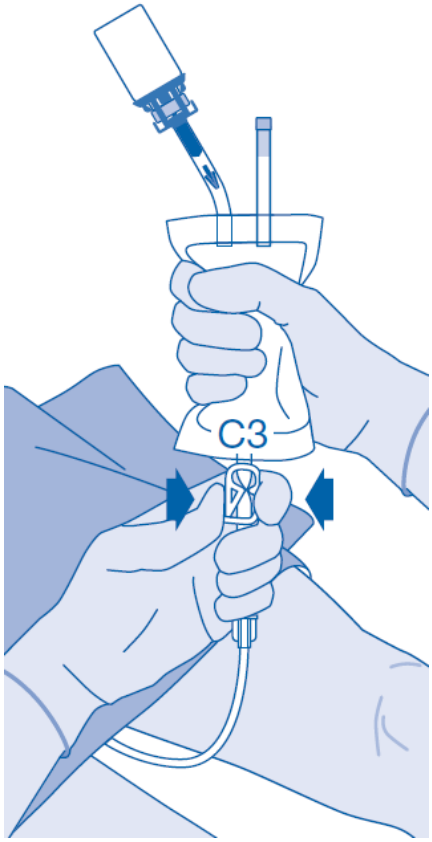
13. Squeeze the remaining air out of the solvent bag to empty the catheter as much as possible.



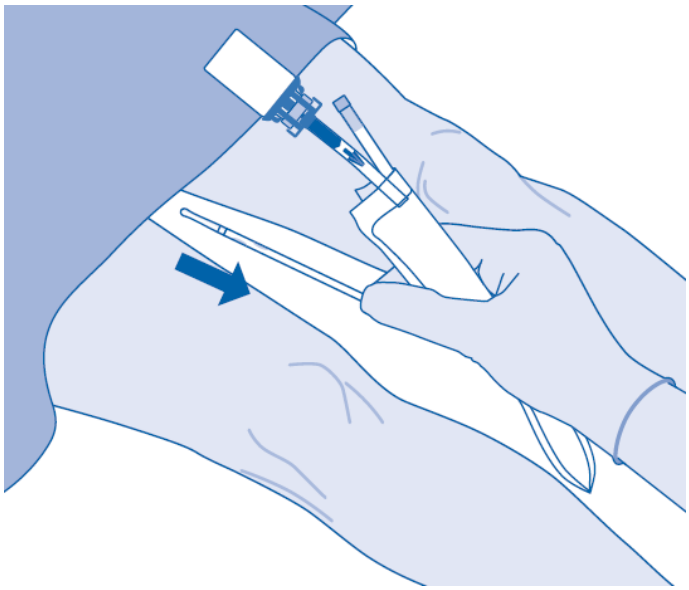
After instillation

14. Closing the pressure clamp (C3) prevents a reflux of fluid into the catheter and minimises the risk of contamination. Alternatively, you can keep the solvent bag compressed while performing

steps 15 and 16.

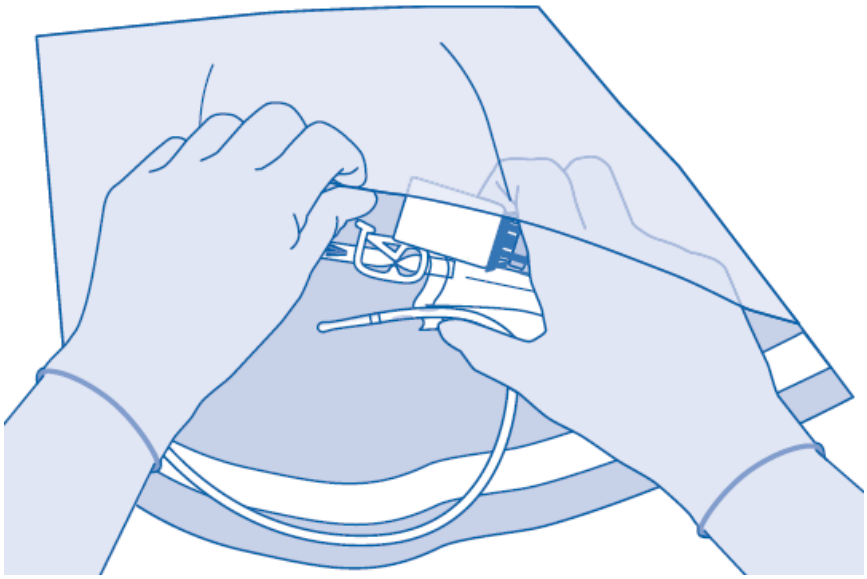


15. Remove the catheter **carefully** from the bladder without disconnecting the solvent bag from the catheter. Avoid contamination from splashing droplets.



16. Dispose of the product according to national regulations using the disposal bag.

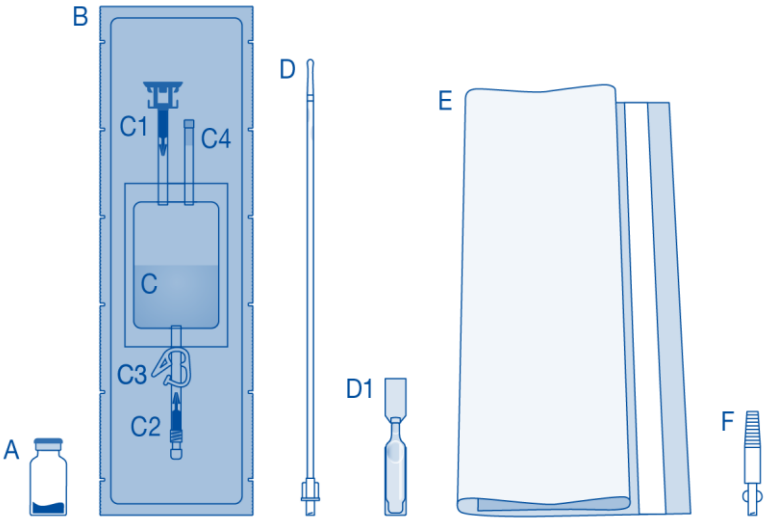
    The contents of the vial are intended for single use/single dose only. Any remaining suspension must be disposed of.



Instructions for users of BCG-medac

Constituents and application of the instillation set <with catheter and Luer-Lock to conical connector>

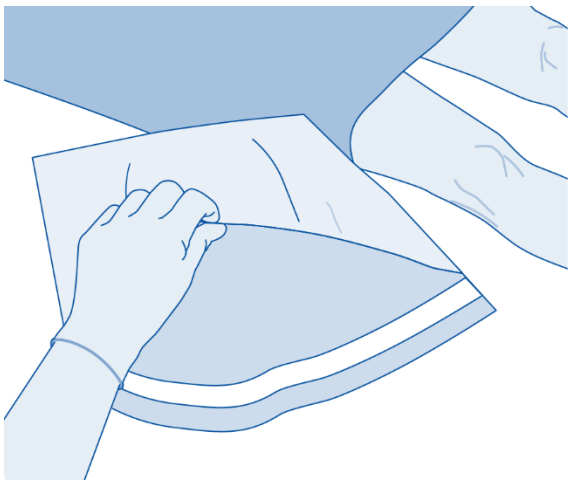
Main constituents of the instillation set



Main constituent	Description
A	Vial with powder
B	Protective cover
C	Solvent bag with 0.9% (9 mg/mL) sodium chloride solution
C1	Vial connector with protective cap and break-open seal
C2	Luer-Lock catheter connector with protective cap and break-open seal
C3	Pressure clamp
C4	Filling port without application function
D	Luer-Lock catheter
D1	Lubricant
E	Disposal bag
F	Luer-Lock to conical connector

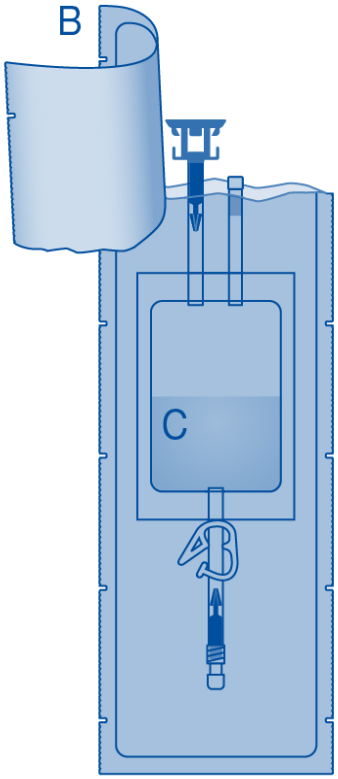
Connecting the vial to the solvent bag

1. Lay out the disposal bag (E) ready for direct disposal of the set after instillation to prevent contamination.

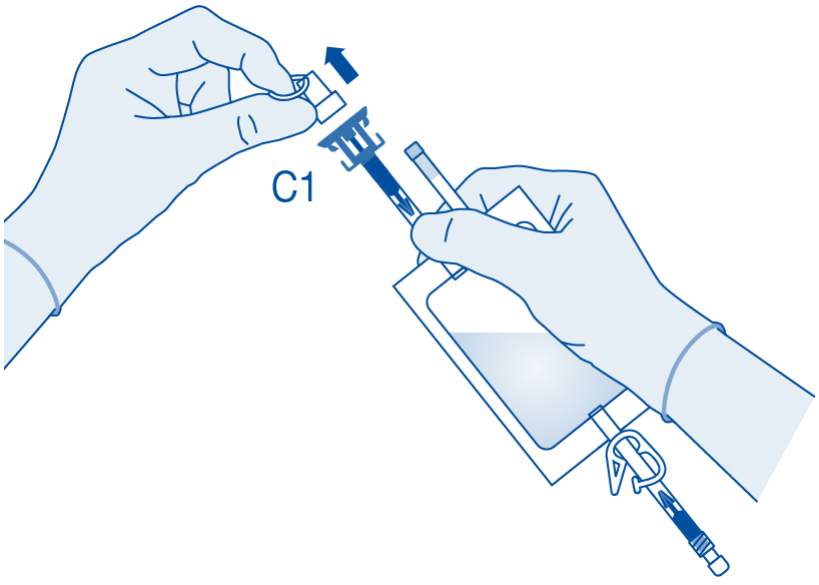


2. Remove the flip-off cap from the vial (A) and disinfect the stopper according to local regulations.

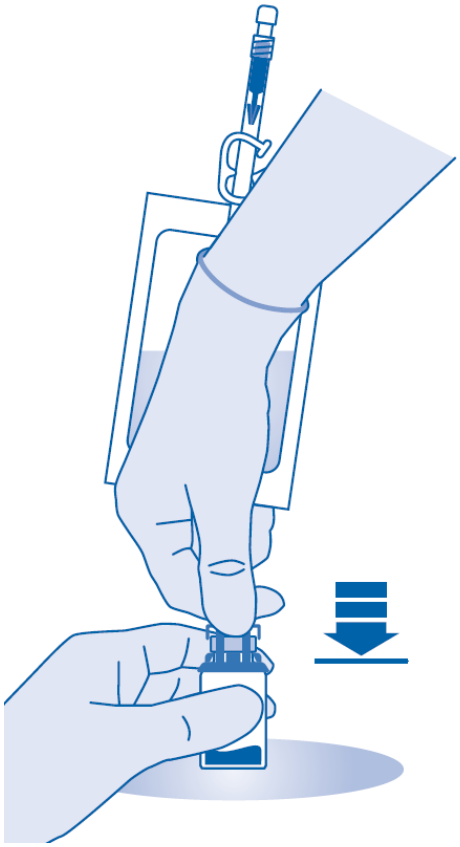
3. Tear open the protective cover (B) of the solvent bag (C) and remove the protective cover completely.



4. Remove the protective cap from the vial connector (C1).

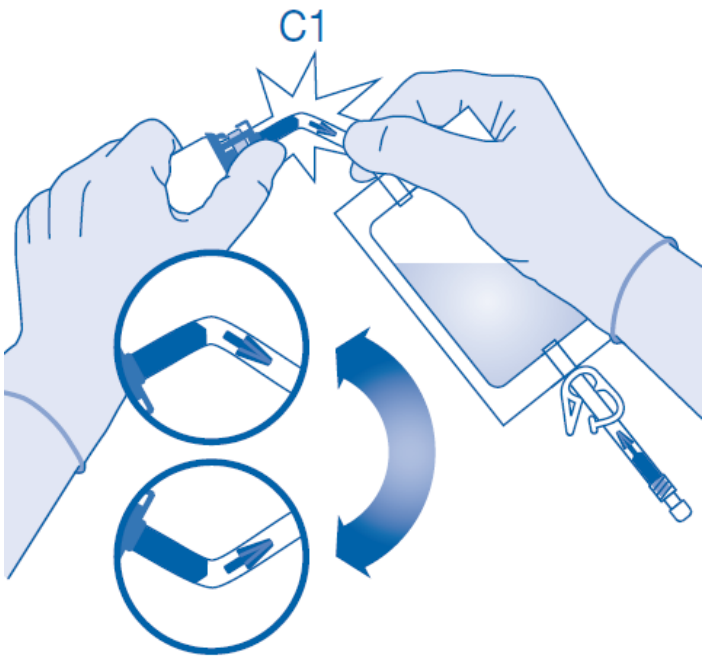


5. Push the connector onto the vial up to the stop.



Mixing the powder with the solvent

6. Bend the break-open seal inside the tube of the vial connector (C1) up and down multiple times to break the seal.



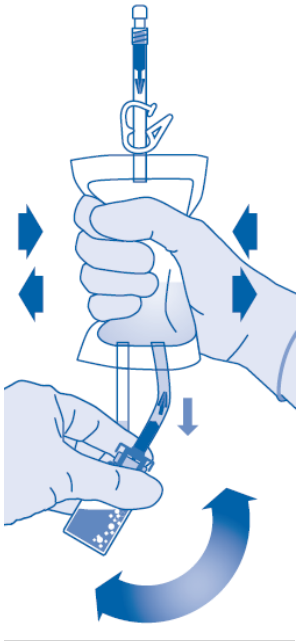
7. Hold the **solvent bag** so that the **vial is below it**.

Squeeze the solvent bag multiple times to transfer enough solvent into the vial.

Make sure that the vial is **not** filled completely to allow for the subsequent transfer of the suspension into the solvent bag. Some solvent may remain inside the bag.

Swirl the vial **slowly** to minimise heavy foaming while mixing the medicinal product with the solvent. If there is a lot of foam, leave the vial to rest briefly (a few minutes).

The contents of the vial have to form a homogeneous suspension. This may take a few minutes.



8. Turn the **solvent bag** upside down and hold it so that the **vial is above it**.

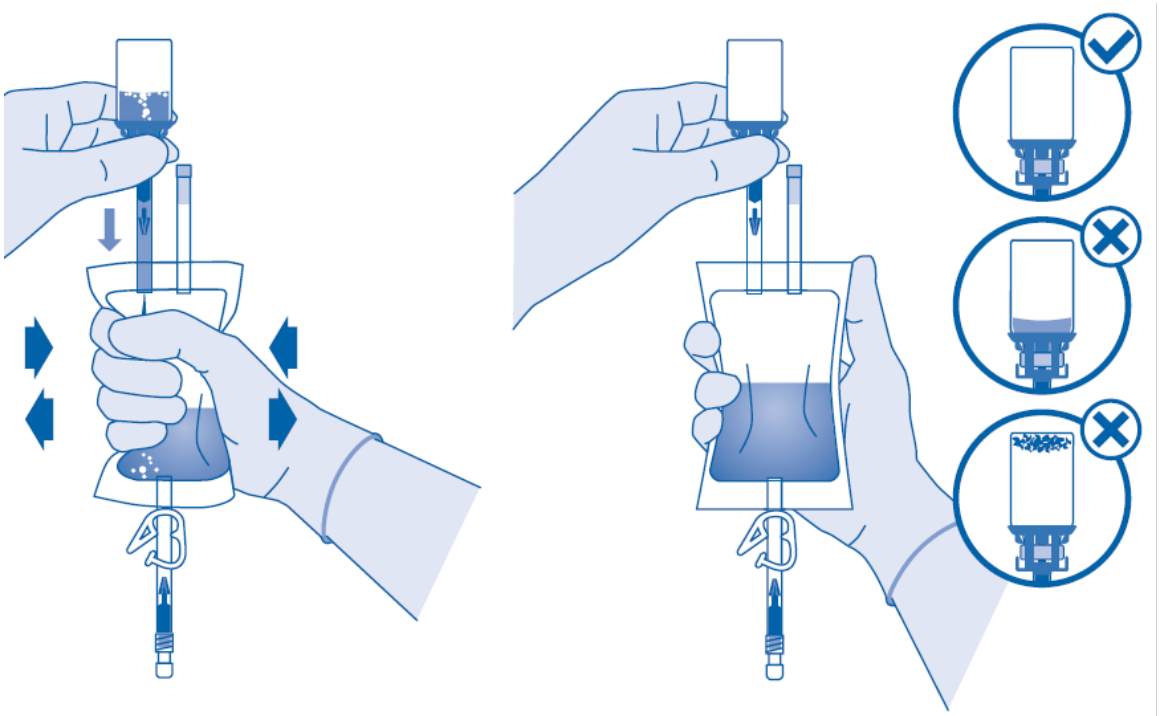
Hold the vial.

Squeeze the solvent bag multiple times until the vial is completely empty.

If any powder remains inside the vial, repeat steps 7 and 8.

From a microbiological point of view the medicinal product should be used immediately. If the medicinal product is not used immediately, please see section 5 “How to store BCG-medac”.

The suspension should not be instilled at refrigerator temperature in order to prevent the patient from feeling the need to urinate resulting in a shortened exposure time.



Catheterisation

9. Catheterise the patient according to local regulations and the instructions for use using the enclosed Luer-Lock catheter (D) and lubricant (D1) or another suitable catheter and/or lubricant.

   Empty the urinary bladder using the catheter.

   Note for use with self-selected catheter with conical connector:
   The enclosed Luer-Lock to conical connector (F) must be used to connect the bag to the self-selected catheter (not shown).

   To do this, the following additional steps must be carried out:
   - Remove the protective cap from the catheter connector (C2, see step 10).
   - Rotate and swirl the bag before connecting to remix any sediments.
   - Connect the Luer-Lock to conical connector (F) to the catheter connector (C2) of the bag.
   - Carefully connect the bag with the connector (F) to the patient's catheter.
   - Then proceed with step 11.

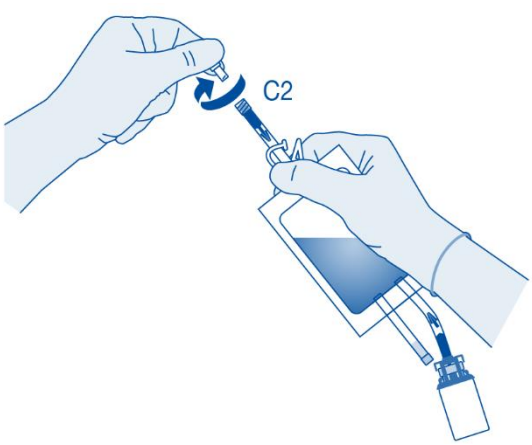
Connecting the catheter to the solvent bag

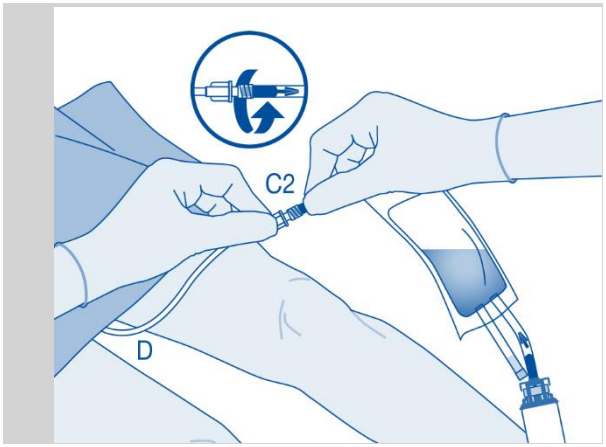
10. To mix any sediments, rotate and swirl the bag before connecting it.

    Do not administer the suspension at refrigerator temperature.

    Remove the protective cap from the catheter connector (C2).

    Connect the patient's Luer-Lock catheter (D) with the catheter connector (C2) of the solvent bag.

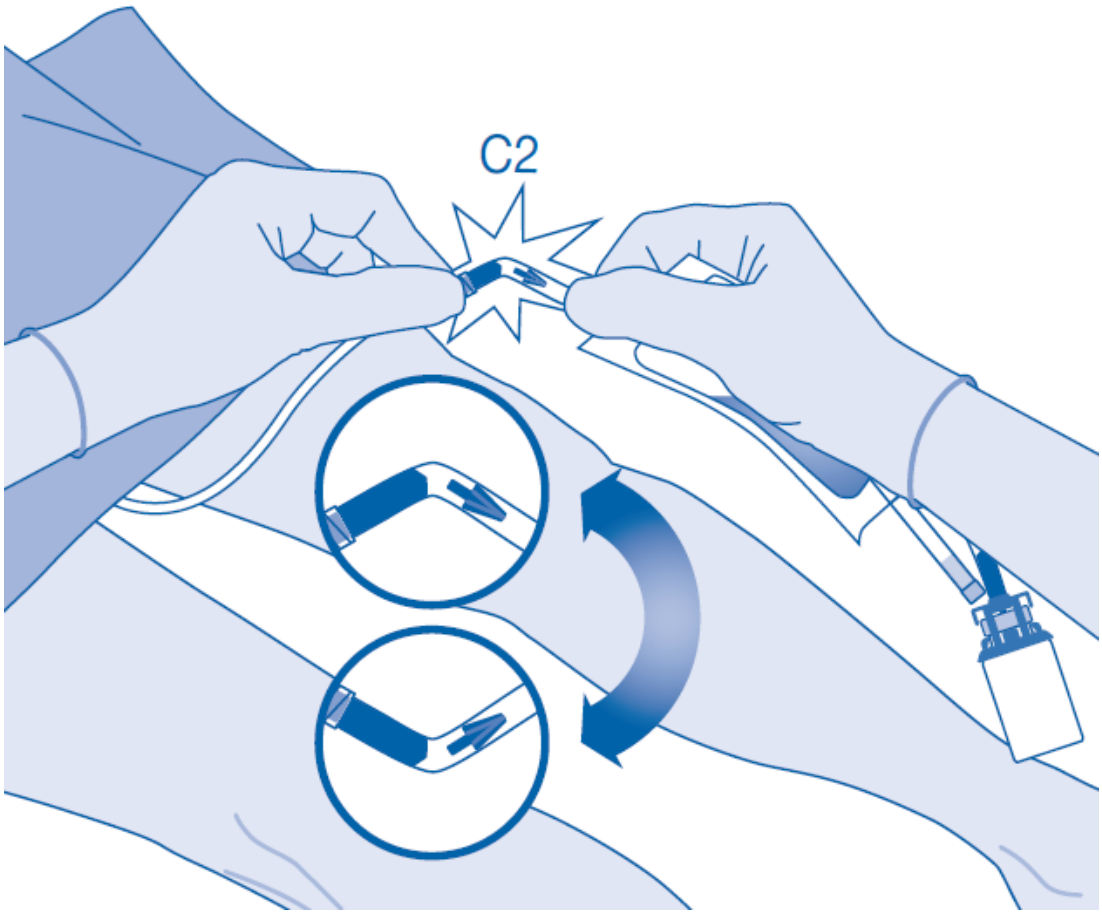




Instillation

11. Bend the break-open seal inside the tube of the catheter connector (C2) up and down multiple times to break the seal.

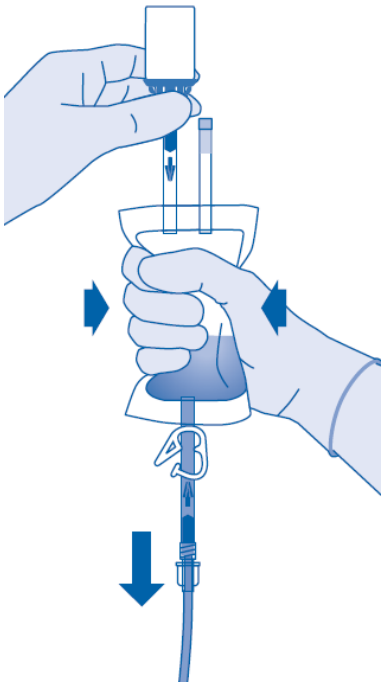
    Hold the patient's catheter steady while doing so.



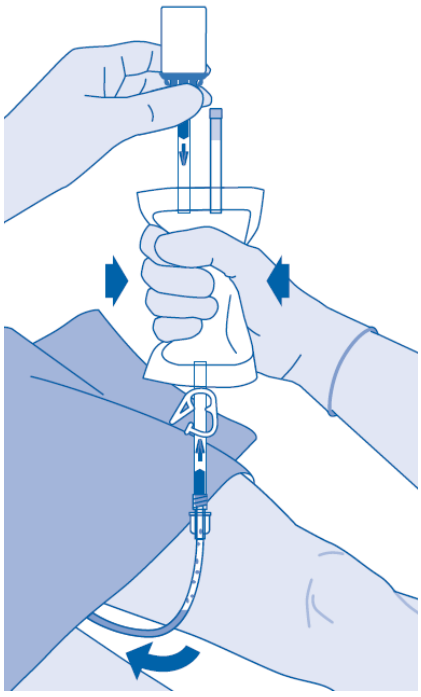
12. Hold the **solvent bag** with the **vial upside down above the bag**.

    Squeeze the solvent bag **gently** with the other hand so that the medicinal product is **slowly** instilled into the patient's urinary bladder.

Continue to squeeze until the solvent bag and the vial are empty.



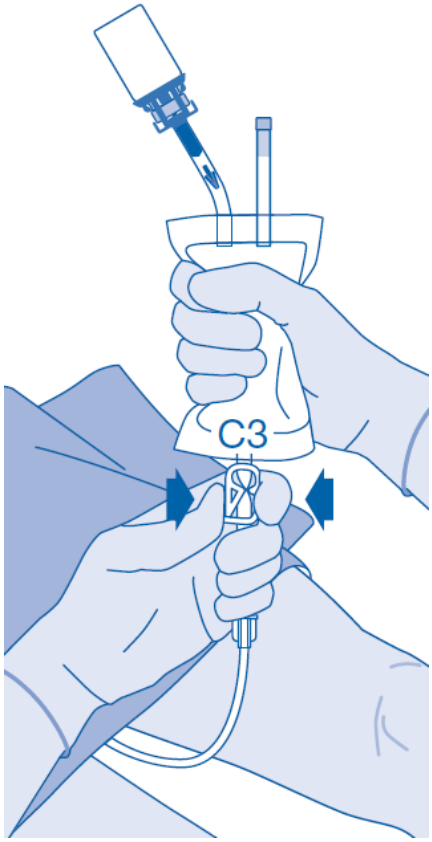
13. Squeeze the remaining air out of the solvent bag to empty the catheter as much as possible.



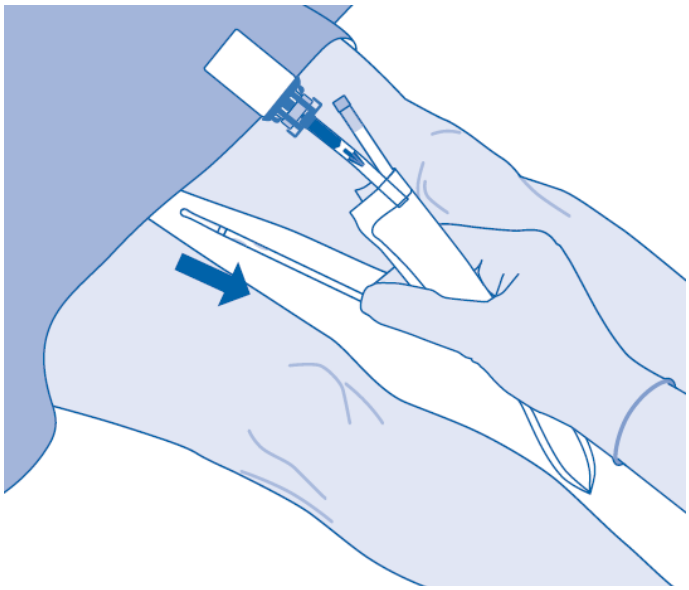
After instillation

14. Closing the pressure clamp (C3) prevents a reflux of fluid into the catheter and minimises the risk of contamination. Alternatively, you can keep the solvent bag compressed while performing

steps 15 and 16.

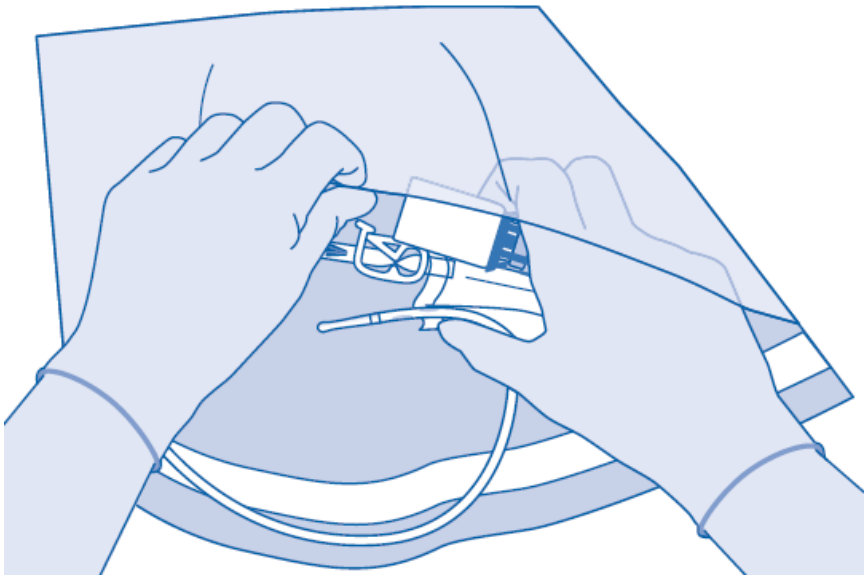


15. Remove the catheter **carefully** from the bladder without disconnecting the solvent bag from the catheter. Avoid contamination from splashing droplets.



16. Dispose of the product according to national regulations using the disposal bag.

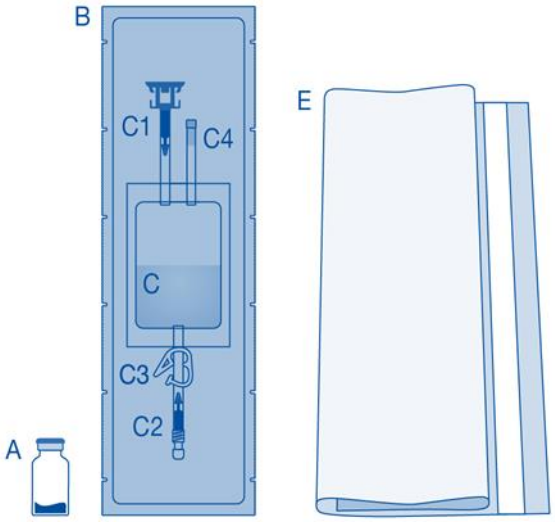
The contents of the vial are intended for single use/single dose only. Any remaining suspension must be disposed of.



Instructions for users of BCG-medac

Constituents and application of the instillation set <without catheter, without Luer-Lock to conical connector>

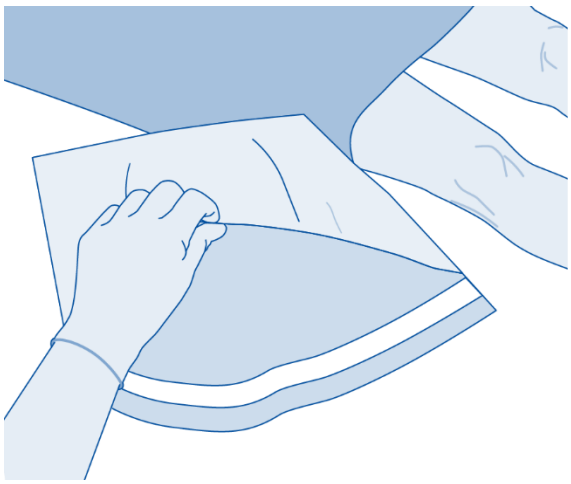
Main constituents of the instillation set



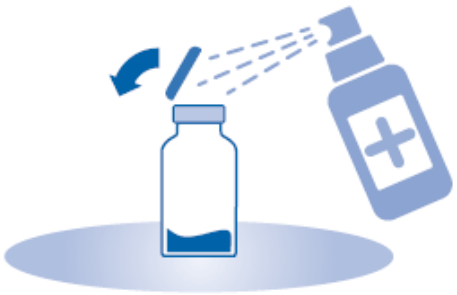
Main constituent	Description
A	Vial with powder
B	Protective cover
C	Solvent bag with 0.9% (9 mg/mL) sodium chloride solution
C1	Vial connector with protective cap and break-open seal
C2	Luer-Lock catheter connector with protective cap and break-open seal
C3	Pressure clamp
C4	Filling port without application function
E	Disposal bag

Connecting the vial to the solvent bag

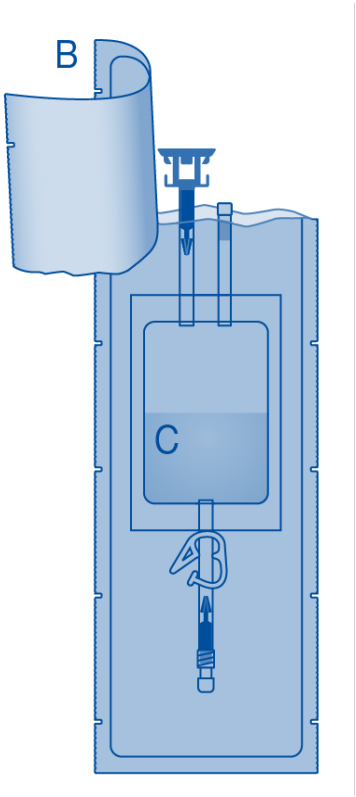
1. Lay out the disposal bag (E) ready for direct disposal of the set after instillation to prevent contamination.



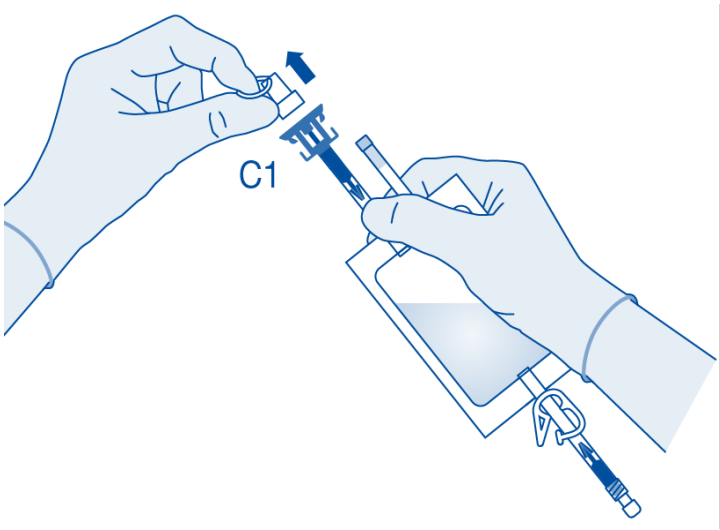
2. Remove the flip-off cap from the vial (A) and disinfect the stopper according to local regulations.



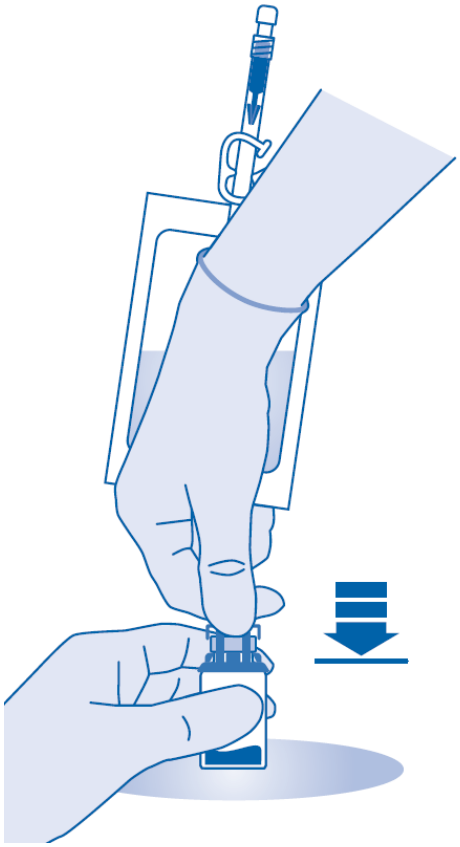
3. Tear open the protective cover (B) of the solvent bag (C) and remove the protective cover completely.



4. Remove the protective cap from the vial connector (C1).

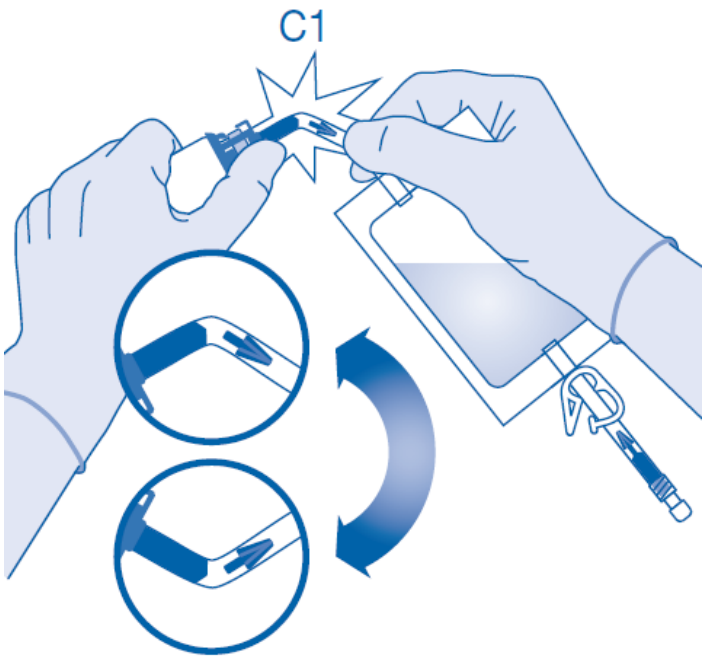


5. Push the connector onto the vial up to the stop.



Mixing the powder with the solvent

6. Bend the break-open seal inside the tube of the vial connector (C1) up and down multiple times to break the seal.



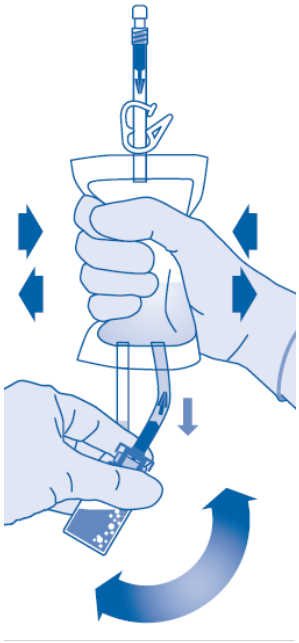
7. Hold the **solvent bag** so that the **vial is below it**.

Squeeze the solvent bag multiple times to transfer enough solvent into the vial.

Make sure that the vial is **not** filled completely to allow for the subsequent transfer of the suspension into the solvent bag. Some solvent may remain inside the bag.

Swirl the vial **slowly** to minimise heavy foaming while mixing the medicinal product with the solvent. If there is a lot of foam, leave the vial to rest briefly (a few minutes).

The contents of the vial have to form a homogeneous suspension. This may take a few minutes.



8. Turn the **solvent bag** upside down and hold it so that the **vial is above it**.

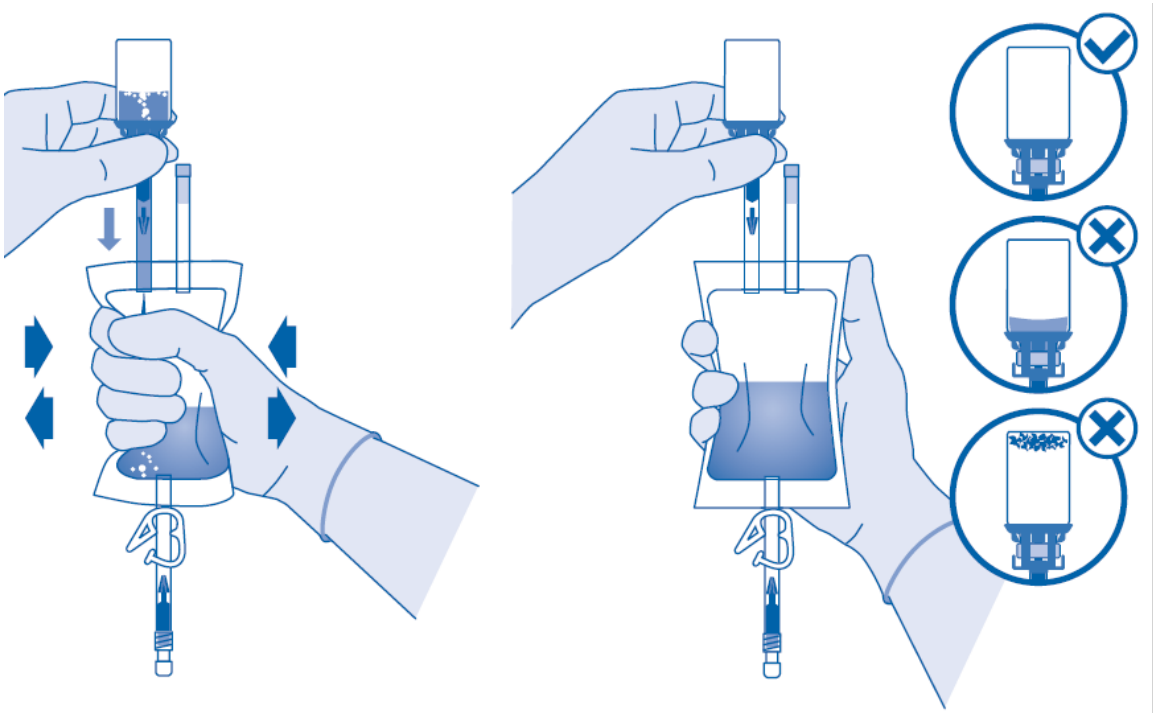
Hold the vial.

Squeeze the solvent bag multiple times until the vial is completely empty.

If any powder remains inside the vial, repeat steps 7 and 8.

From a microbiological point of view the medicinal product should be used immediately. If the medicinal product is not used immediately, please see section 5 “How to store BCG-medac”.

The suspension should not be instilled at refrigerator temperature in order to prevent the patient from feeling the need to urinate resulting in a shortened exposure time.



Catheterisation

9. Catheterise the patient according to local regulations and the instructions for use using a suitable catheter and lubricant.

   Empty the urinary bladder using the catheter.

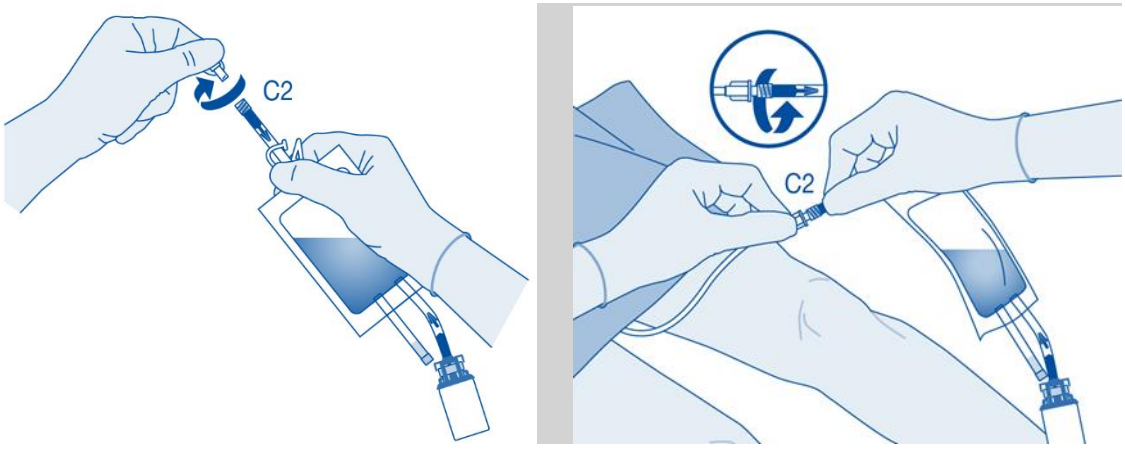
Connecting the catheter to the solvent bag

10. To mix any sediments, rotate and swirl the bag before connecting it.

    Do not administer the suspension at refrigerator temperature.

    Remove the protective cap from the catheter connector (C2).

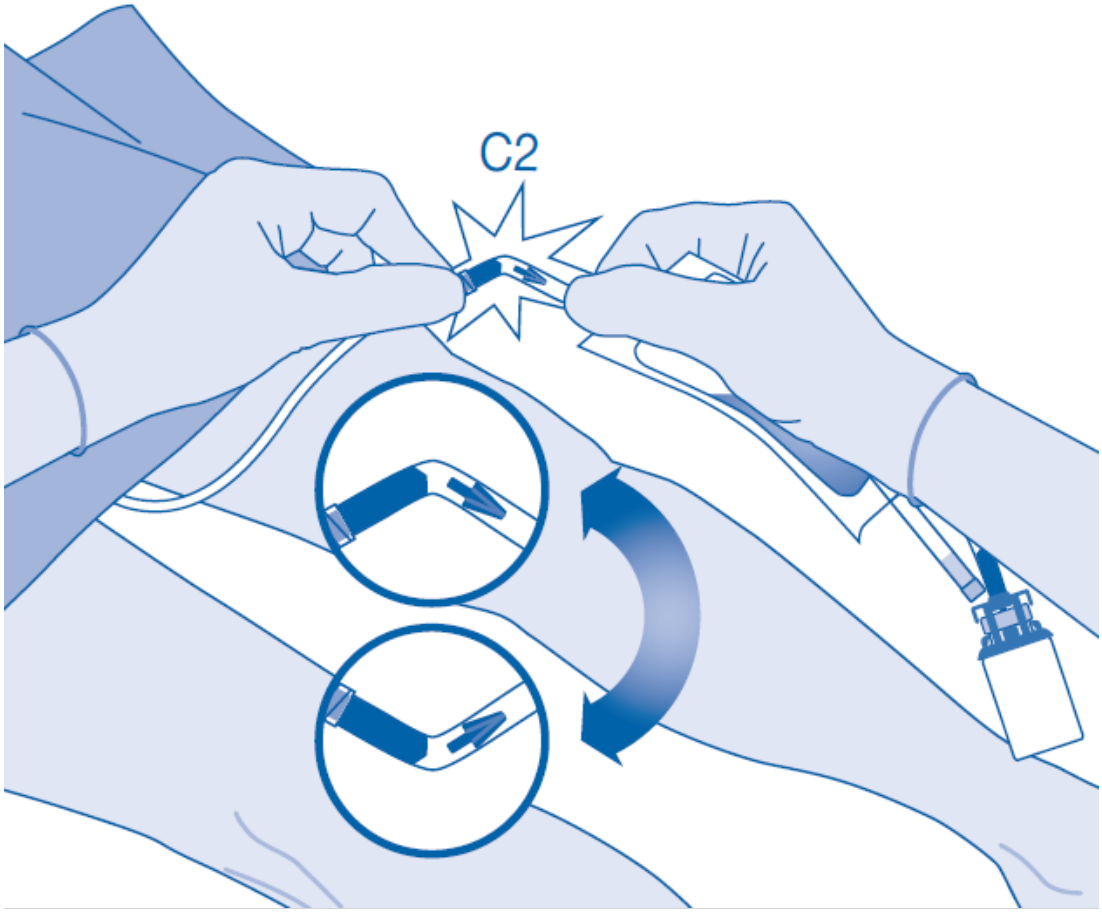
    Connect the patient's catheter with the catheter connector (C2) of the solvent bag.



Instillation

11. Bend the break-open seal inside the tube of the catheter connector (C2) up and down multiple times to break the seal.

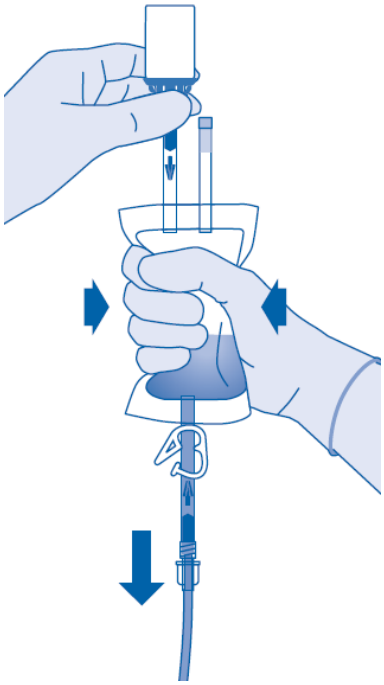
    Hold the patient's catheter steady while doing so.



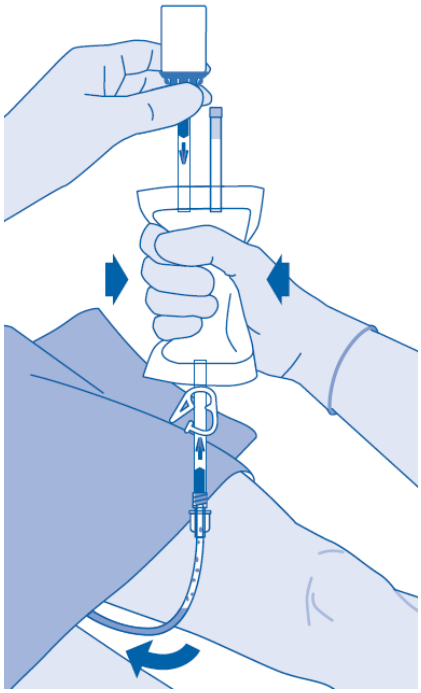
12. Hold the **solvent bag** with the **vial upside down above the bag**.

    Squeeze the solvent bag **gently** with the other hand so that the medicinal product is **slowly** instilled into the patient's urinary bladder.

    Continue to squeeze until the solvent bag and the vial are empty.

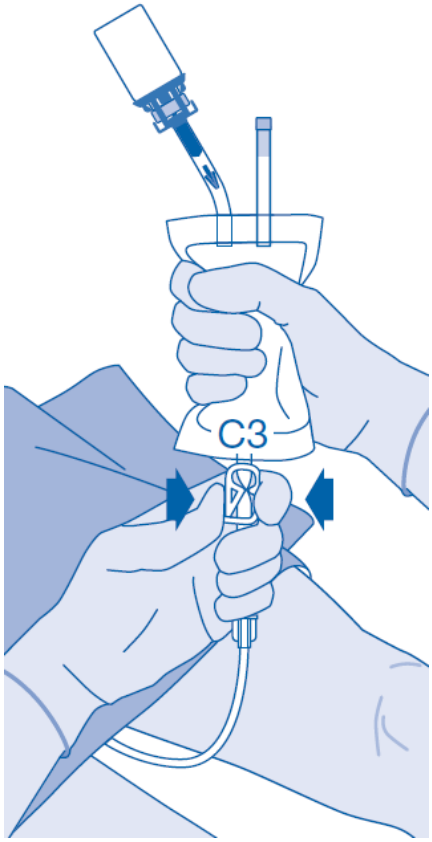


13. Squeeze the remaining air out of the solvent bag to empty the catheter as much as possible.

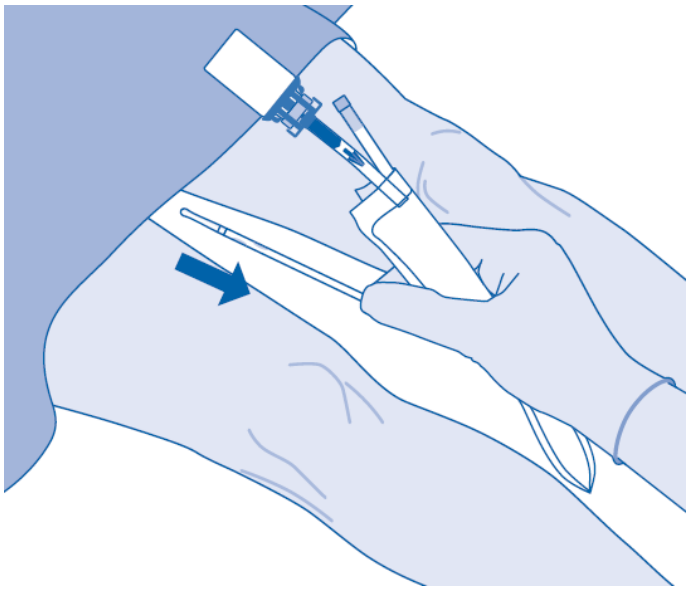


After instillation

14. Closing the pressure clamp (C3) prevents a reflux of fluid into the catheter and minimises the risk of contamination. Alternatively, you can keep the solvent bag compressed while performing steps 15 and 16.

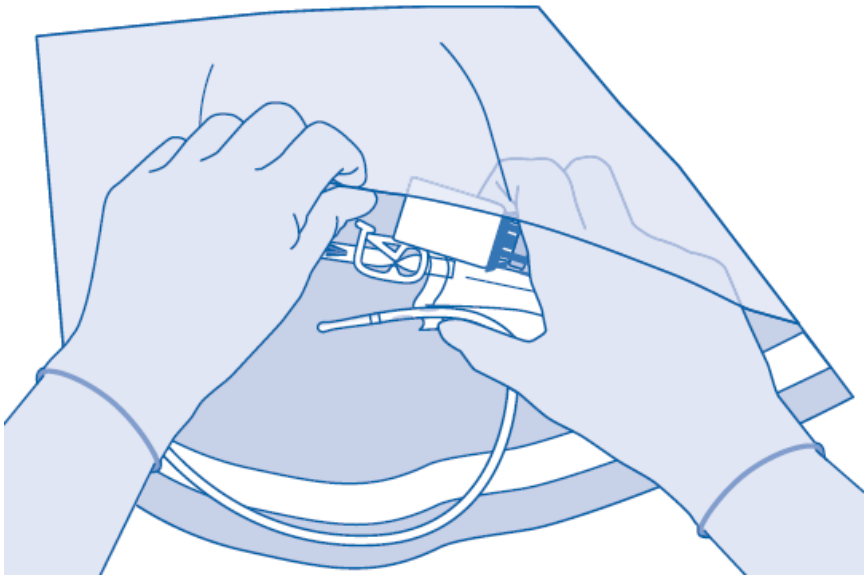


15. Remove the catheter **carefully** from the bladder without disconnecting the solvent bag from the catheter. Avoid contamination from splashing droplets.



16. Dispose of the product according to national regulations using the disposal bag.

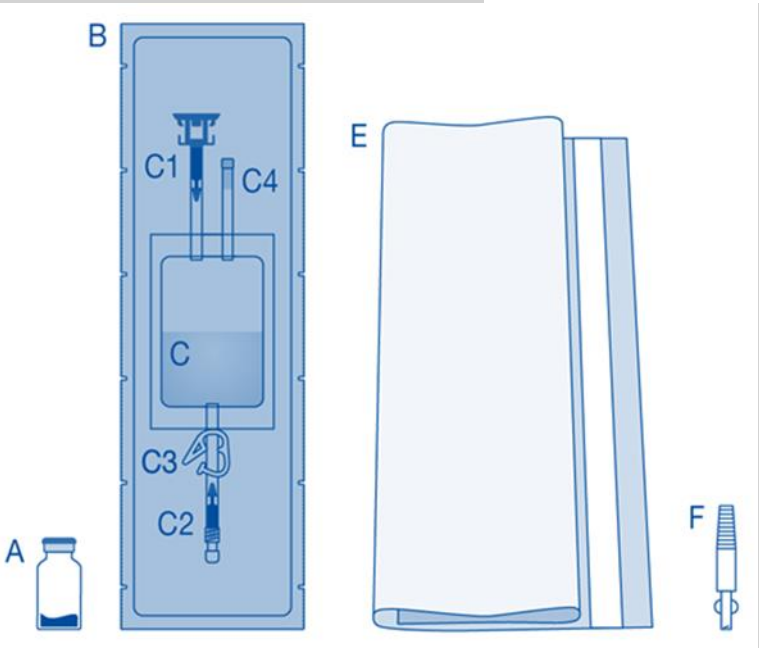
    The contents of the vial are intended for single use/single dose only. Any remaining suspension must be disposed of.



Instructions for users of BCG-medac

Constituents and application of the instillation set <without catheter, with Luer-Lock to conical connector>

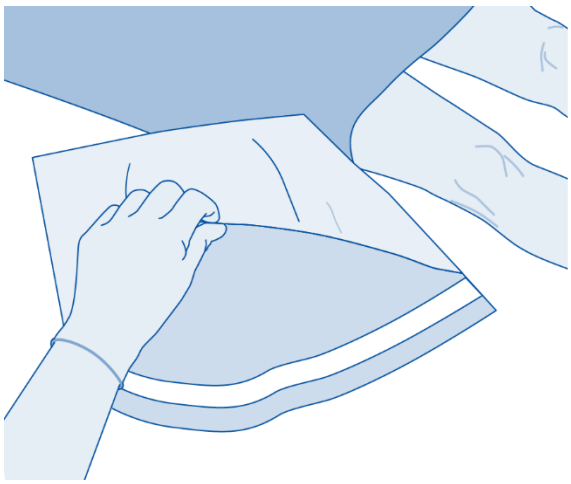
Main constituents of the instillation set



Main constituent	Description
A	Vial with powder
B	Protective cover
C	Solvent bag with 0.9% (9 mg/mL) sodium chloride solution
C1	Vial connector with protective cap and break-open seal
C2	Luer-Lock catheter connector with protective cap and break-open seal
C3	Pressure clamp
C4	Filling port without application function
E	Disposal bag
F	Luer-Lock to conical connector

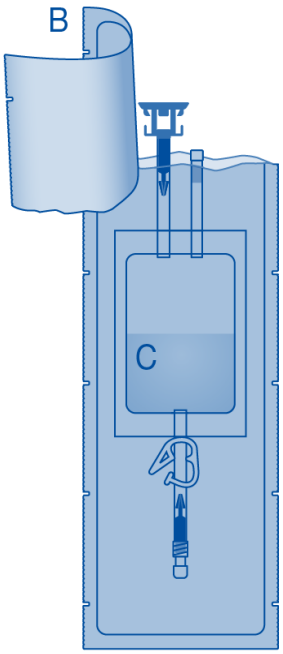
Connecting the vial to the solvent bag

1. Lay out the disposal bag (E) ready for direct disposal of the set after instillation to prevent contamination.

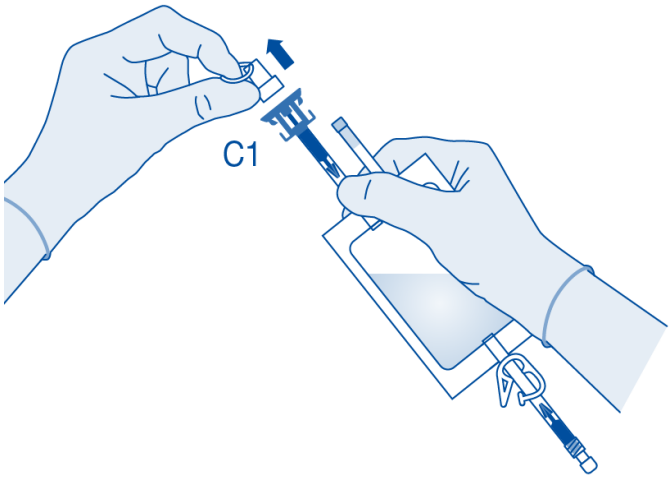


2. Remove the flip-off cap from the vial (A) and disinfect the stopper according to local regulations.

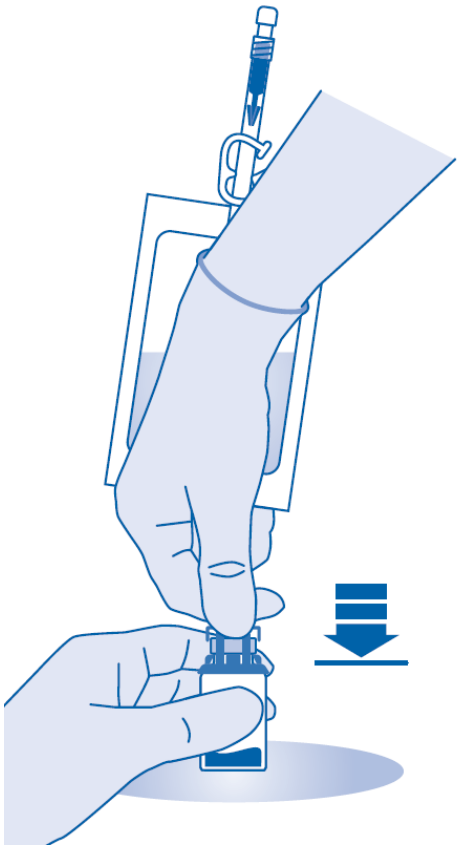
3. Tear open the protective cover (B) of the solvent bag (C) and remove the protective cover completely.



4. Remove the protective cap from the vial connector (C1).

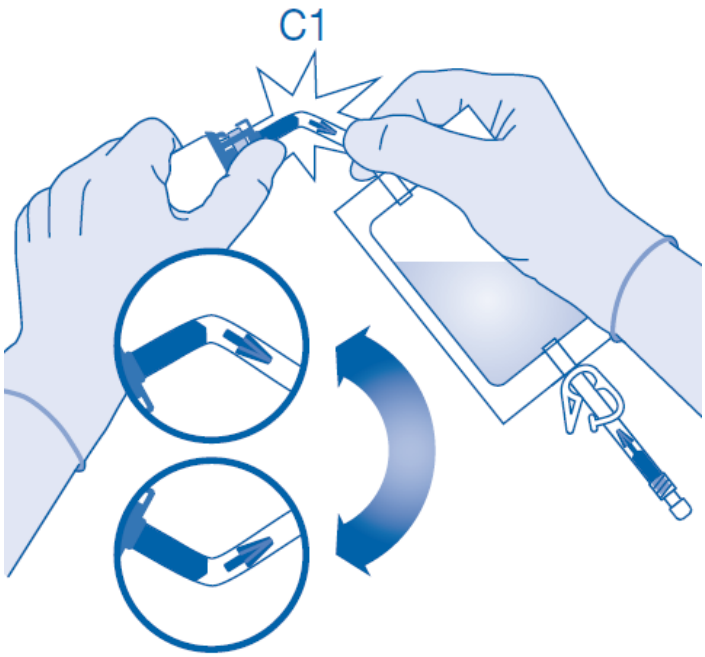


5. Push the connector onto the vial up to the stop.



Mixing the powder with the solvent

6. Bend the break-open seal inside the tube of the vial connector (C1) up and down multiple times to break the seal.



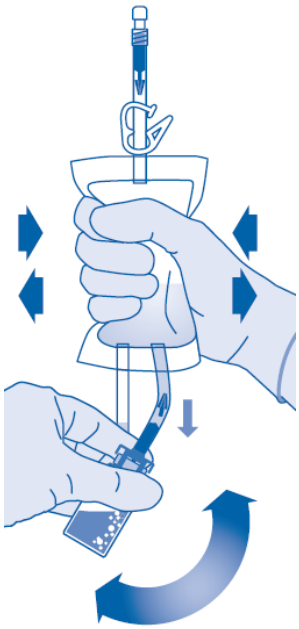
7. Hold the **solvent bag** so that the **vial is below it**.

Squeeze the solvent bag multiple times to transfer enough solvent into the vial.

Make sure that the vial is **not** filled completely to allow for the subsequent transfer of the suspension into the solvent bag. Some solvent may remain inside the bag.

Swirl the vial **slowly** to minimise heavy foaming while mixing the medicinal product with the solvent. If there is a lot of foam, leave the vial to rest briefly (a few minutes).

The contents of the vial have to form a homogeneous suspension. This may take a few minutes.



8. Turn the **solvent bag** upside down and hold it so that the **vial is above it**.

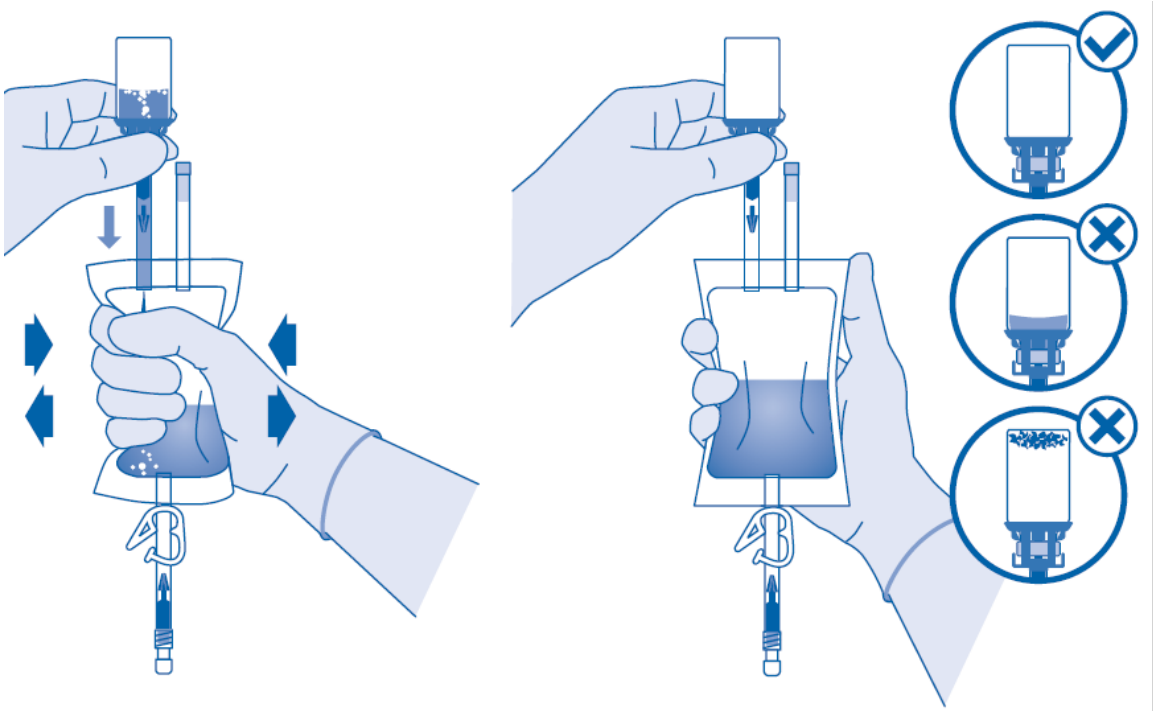
Hold the vial.

Squeeze the solvent bag multiple times until the vial is completely empty.

If any powder remains inside the vial, repeat steps 7 and 8.

From a microbiological point of view the medicinal product should be used immediately. If the medicinal product is not used immediately, please see section 5 “How to store BCG-medac”.

The suspension should not be instilled at refrigerator temperature in order to prevent the patient from feeling the need to urinate resulting in a shortened exposure time.



Catheterisation

9. Catheterise the patient according to local regulations and the instructions for use using a suitable catheter and lubricant.

Empty the urinary bladder using the catheter.

This pack does not contain a catheter. Use the enclosed connector (F) to connect the bag to the patient’s catheter with a conical connector (not shown).

To do this, the following additional steps must be carried out:
- Remove the protective cap from the catheter connector (C2, see step 10).
- Connect the connector (F) to the catheter connector (C2) of the bag.
- Carefully connect the bag with the connector (F) to the patient’s catheter.
- Then proceed with step 11.

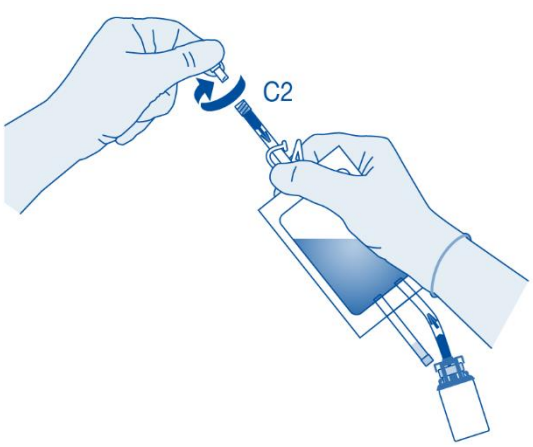
Connecting the catheter to the solvent bag

10. To mix any sediments, rotate and swirl the bag before connecting it.

    Do not administer the suspension at refrigerator temperature.

    Remove the protective cap from the catheter connector (C2).

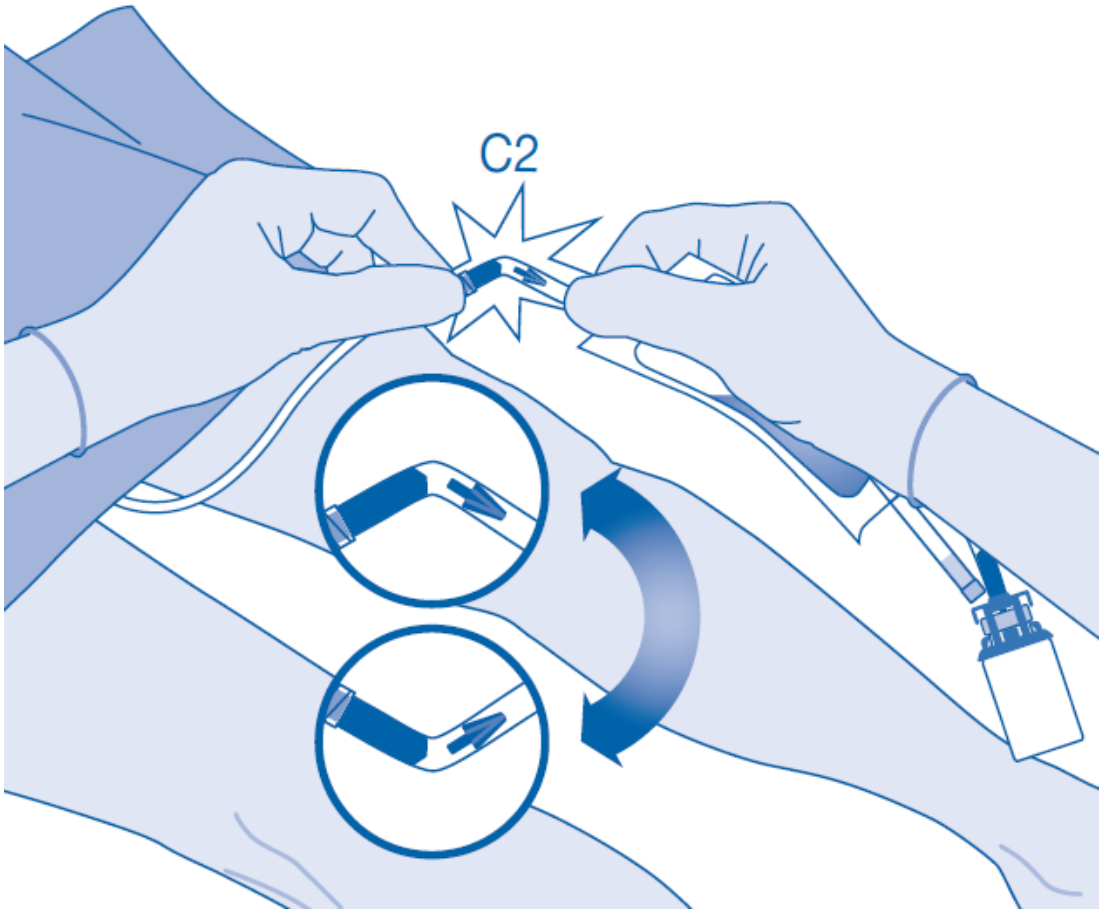
    Connect the patient's catheter with the catheter connector (C2) of the solvent bag.



Instillation

11. Bend the break-open seal inside the tube of the catheter connector (C2) up and down multiple times to break the seal.

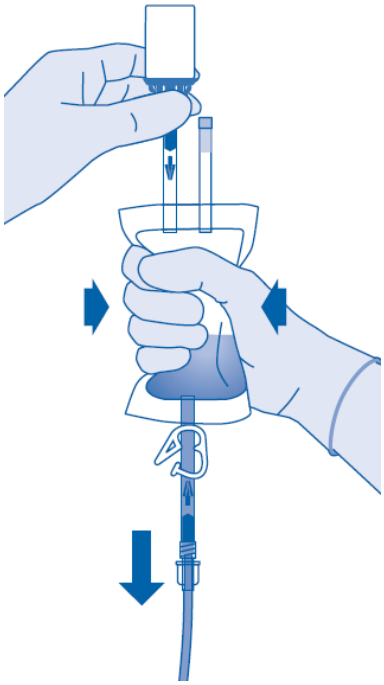
    Hold the patient's catheter steady while doing so.



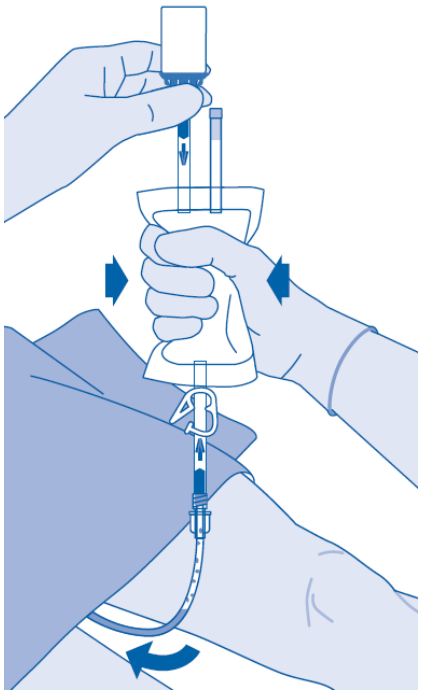
12. Hold the **solvent bag** with the **vial upside down above the bag**.

Squeeze the solvent bag **gently** with the other hand so that the medicinal product is **slowly** instilled into the patient's urinary bladder.

Continue to squeeze until the solvent bag and the vial are empty.

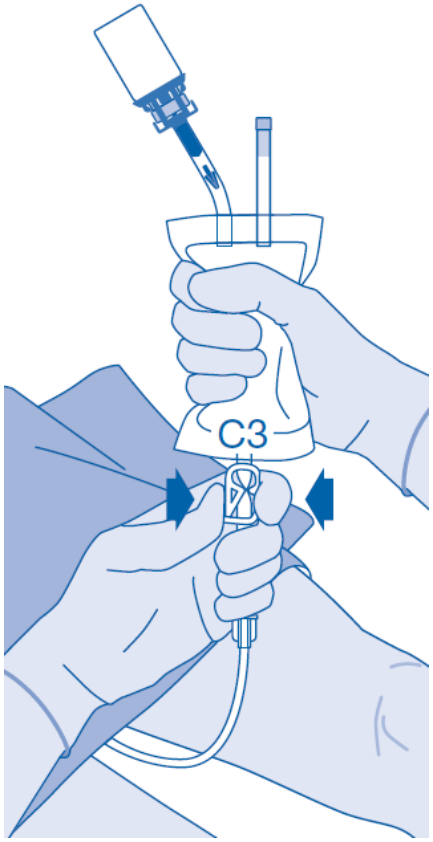


13. Squeeze the remaining air out of the solvent bag to empty the catheter as much as possible.

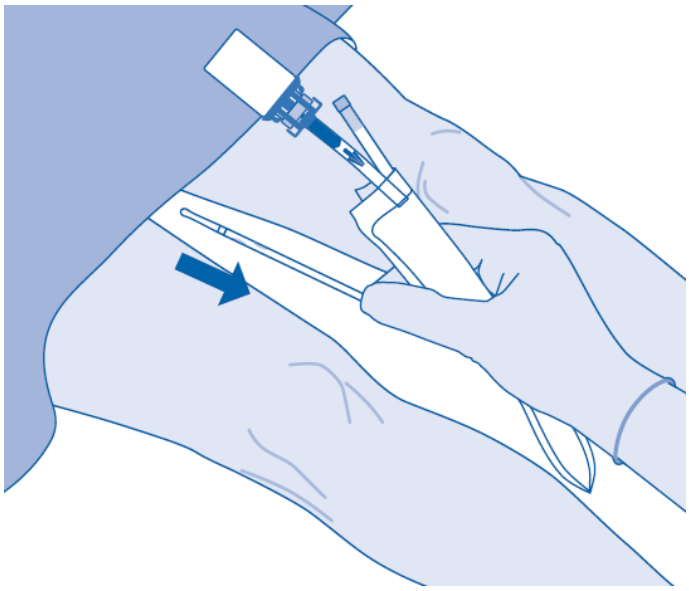


After instillation

14. Closing the pressure clamp (C3) prevents a reflux of fluid into the catheter and minimises the risk of contamination. Alternatively, you can keep the solvent bag compressed while performing steps 15 and 16.



15. Remove the catheter **carefully** from the bladder without disconnecting the solvent bag from the catheter. Avoid contamination from splashing droplets.



16. Dispose of the product according to national regulations using the disposal bag.

The contents of the vial are intended for single use/single dose only. Any remaining suspension must be disposed of.