

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

BCG-medac $2 \times 10^8 - 1.5 \times 10^9$ cfu Powder and solvent for intravesical suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

After reconstitution, one vial contains:

BCG (Bacillus Calmette Guérin) bacteria derived from *Mycobacterium bovis*, seed RIVM derived from seed 1173-P2, viable units 2×10^8 to 1.5×10^9

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder and solvent for intravesical suspension

Powder:

White or almost white powder or porous cake with shades of yellow and grey

Solvent:

Colourless, clear solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

BCG-medac is indicated for:

- the treatment of primary or concurrent carcinoma-in-situ of the urinary bladder
- the prevention of recurrence of high-risk non-muscle invasive urothelial bladder carcinoma (pTaG3, pT1G2, pT1G3) after transurethral resection
- the treatment and/or the prevention of recurrence of aggressive variants of urothelial carcinoma, for example micropapillary or nested variants.

4.2 Posology and method of administration

BCG-medac must be administered by physicians experienced in this therapy.

BCG-medac is intended for intravesical use following reconstitution. For instructions on reconstitution of the BCG-medac suspension before administration, see section 6.6.

Posology

Adults and the elderly

The content of one vial, reconstituted and diluted as indicated, is required for one instillation into the urinary bladder.

Induction therapy

BCG therapy should begin about 2 – 3 weeks after transurethral resection (TUR) or bladder biopsy. Treatment should not be started until mucosal lesions after TUR have healed. Treatment should also be delayed in cases of gross haematuria or major bladder irritability. Care should be taken to avoid traumatic catheterisation for BCG therapy.

Induction is weekly instillation of BCG-medac for 6 weeks. This should be followed by maintenance therapy, described below.

Maintenance therapy

Maintenance treatment consists of 3 instillations at weekly intervals given at months 3, 6, 12 after initiation of treatment. Maintenance treatment could continue at 6-monthly intervals for up to 3 years, if appropriate.

Although maintenance therapy reduces recurrence and may reduce progression, the adverse reactions and discomfort of the treatment may outweigh the benefits for some patients. Thus, benefit-risk assessment and consideration of patient preferences is important before beginning or continuing maintenance treatment. The need for maintenance treatment every 6 months beyond the first year of treatment should further be evaluated on the basis of tumour classification and clinical response.

Paediatric population

The safety and efficacy of BCG-medac in children have not been established. No data are available.

Method of administration

The patient should not drink any fluid for a period of 4 hours before the instillation until 2 hours after instillation.

A urethral catheter is inserted into the bladder under aseptic conditions. A sufficient quantity of lubricant should be used to reduce the chance of traumatising the urinary mucosa and therefore the risk of severe complications and also to reduce discomfort for the patient. The bladder must be emptied before BCG instillation.

BCG-medac is instilled into the bladder via the urethral at low pressure. The instilled BCG-medac suspension must remain in the bladder for a period of 2 hours if possible. During this period the suspension should have sufficient contact with the entire mucosal surface of the bladder, therefore, the patient should be mobilised as much as possible or, in case of a bed-ridden patient, should be turned over from back to abdomen and vice versa every 15 minutes. After 2 hours, the patient should void the instilled suspension in a sitting position.

Urine should be voided in a sitting position for 6 hours after treatment and two cups of household bleach should be added to the toilet before flushing. The bleach and urine should be left to stand in the toilet for 15 minutes before flushing.

For the 48 hours following each instillation, advise patients to drink more water than usual to achieve hyper-hydration, if possible.

Patients treated with BCG-medac should be given the package leaflet and the patient alert card.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

BCG-medac should not be used in immunosuppressed patients with congenital or acquired immune deficiencies, whether due to concurrent disease (e.g., positive HIV serology, leukaemia, lymphoma), cancer therapy (e.g., cytostatic medicinal products, radiation) or immunosuppressive therapy (e.g., corticosteroids).

BCG-medac should not be administered to patients with active tuberculosis or on anti-tuberculosis drugs. The risk of active tuberculosis must be ruled out from the medical history and, if indicated, by diagnostic tests according to local guidelines.

Past history of radiotherapy to the bladder.

Treatment with BCG-medac is contraindicated in women during lactation and pregnancy (see section 4.6).

BCG-medac must not be instilled before 2 to 3 weeks after a TUR, a bladder biopsy or a traumatic catheterisation.

Perforation of the bladder which might result in increased risk of severe systemic infections (see section 4.4).

Acute urinary tract infection (see section 4.4). Asymptomatic, isolated leukocyturia and asymptomatic bacteriuria are not contraindications for intravesical therapy with BCG-medac, and antibiotic prophylaxis is not necessary.

4.4 Special warnings and precautions for use

BCG-medac must not be used subcutaneously, intradermally, intramuscularly or intravenously or for vaccination.

Handling precautions

BCG-medac should not be handled either in the same room or by the same personnel preparing cytotoxic medicinal products for intravenous administration. BCG-medac should not be handled by a person with immunodeficiency. Contact of BCG-medac with skin and mucosa should be avoided. Contamination can lead to hypersensitivity reaction or infection of the concerned area.

Spillage of BCG-medac

Spillage of BCG-medac suspension should be treated with a disinfectant with proven activity against mycobacteria, such as household bleach. Spillage on the skin should be treated with an appropriate disinfectant.

General hygiene for the patient

It is recommended to wash hands and genital area after micturition. This applies especially to the first micturitions following BCG instillation. If skin lesions are contaminated, the use of an appropriate disinfectant is recommended.

Tuberculin cutaneous tests

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, a Tuberculin test (PPD) should be performed before administration of BCG-medac.

Detection of Bacillus Calmette Guérin

Physicians should be aware that detection of BCG bacteria from a biopsy is difficult and negative results do not rule out a systemic infection. In several cases BCG detection was not successful even though the patient experienced a systemic infection. The available methods (microscopy, PCR and/or cultures and/or a detection of tuberculosis-compatible histology) are not reliable.

Severe systemic BCG infections/reactions

Traumatic instillation could promote BCG-septicaemic events with possible septic shock and a life-threatening situation. For treatment options see section 4.8.

Urinary tract infection should be excluded before each bladder instillation of BCG (bladder mucous membrane inflammation may increase the risk of haematological dissemination of BCG). If a urinary tract infection is diagnosed during BCG therapy, the therapy should be interrupted until the urinalysis is normalised and treatment with antibiotics is completed.

The possibility of severe systemic BCG-infections with the necessity of anti-tuberculosis therapy has to be considered before starting the BCG therapy, especially in elderly patients (see Elderly patients) and patients with hepatic impairment.

Severe systemic BCG infections/reactions have been reported in less than 5 %. For signs and symptoms please refer to section 4.8.

If a systemic BCG infection is suspected, a physician specialised in infectious diseases should be consulted. BCG-infection can be potentially fatal. For further information please refer to section 4.8.

Reiter's syndrome presents as a mainly immuno-mediated reaction, which is not necessarily caused by disseminated BCG but could also be triggered by BCG localised in the urinary tract system.

Fever or gross haematuria

Treatment should be postponed until resolution of concurrent fever or gross haematuria.

Low bladder capacity

The risk of bladder contracture may increase in patients with low bladder capacity.

HLA-B27

Patients with positive HLA-B27 could have an increase of the occurrence of reactive arthritis or Reiter's syndrome.

Flare-up of latent BCG infection (including delayed diagnosis)

There have been single case reports in which BCG bacteria persisted in the body for several years. Latent tuberculosis infections might flare-up years after the initial infection, arising especially from granulomatous pneumonitis, abscesses, infected aneurysms, infection of an implant, graft or the surrounding tissue.

The patient has to be made aware of the possibility of late flare-up of latent BCG-infections and educated regarding the actions if symptoms like fever and weight loss of unknown origin occur.

Please note that a patient alert card with focus on this topic is available in the packaging and must be handed over to the patient.

In case of suspicion of a flare-up of latent tuberculosis, a physician specialised in infectious diseases should be consulted.

Elderly patients

BCG administration in elderly patients is not contraindicated. However, the risk of a systemic BCG infection/reaction should be considered before the first administration is performed. Elderly patients may suffer from renal or hepatic impairment which could have an influence on the treatment with anti-tuberculosis medicinal products in case of severe systemic BCG infection/reaction. Caution should also be exercised in elderly patients with reduced general condition.

Patients with contact to immunosuppressed persons

Patients treated with BCG-medac should employ adequate hygienic measures if in contact with immunosuppressed patients. *Mycobacterium bovis* is less pathogenic than *Mycobacterium tuberculosis* and man-to-man transmission has not been reported yet, but it cannot be excluded especially in immunosuppressed patients.

Sexual transmission

Sexual transmission of BCG has not been reported yet, but it is recommended to refrain from intercourse or use a condom for one week after BCG therapy.

4.5 Interaction with other medicinal products and other forms of interaction

BCG-medac is sensitive to most antibiotics and in particular to anti-tuberculosis medicinal products (e.g., ethambutol, streptomycin, p-aminosalicylic acid [PAS], isoniazid [INH] and rifampicin). Resistance against pyrazinamide and cycloserine has been described.

During intravesical BCG instillation therapy, simultaneous administration of anti-tuberculosis agents and antibiotics like fluoroquinolones, doxycycline or gentamicin should be avoided due to sensitivity of BCG to those medicinal products. If a patient is being treated with an antibiotic, it is recommended to postpone the intravesical instillation until the end of the antibiotic-treatment (see also "Contraindications").

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of BCG in pregnant women. Reproductive animal studies were not performed. BCG-medac is not recommended during pregnancy.

Breast-feeding

There is insufficient information on the excretion of BCG/metabolites in human milk. BCG-medac is contraindicated during breast-feeding (see section 4.3).

Fertility

Intravesical BCG therapy was found to adversely affect spermatogenesis and might cause oligospermia or azoospermia. Animal studies are insufficient with respect to reproductive toxicity. However, men should seek advice about the possibility of sperm preservation before starting therapy.

4.7 Effects on ability to drive and use machines

Local or systemic symptoms during therapy with BCG-medac could affect the ability to drive or operate machines.

4.8 Undesirable effects

Undesirable effects are listed below by system organ class and frequency. Frequencies below are defined as: Very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$) or not known (cannot be estimated from the available data).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System organ class	Frequency and undesirable effects
Infections and infestations	<u>Very common</u> Cystitis and inflammatory reactions (granuloma) of the bladder, asymptomatic granulomatous prostatitis
	<u>Uncommon</u> Urinary tract infection, orchitis, epididymitis, symptomatic granulomatous prostatitis, severe systemic BCG reaction/infection, BCG sepsis, miliary pneumonitis, skin abscess, Reiter's syndrome (conjunctivitis, asymmetrical oligoarthritis and cystitis)
	<u>Rare</u> Vascular infection (e.g. infected aneurysm), renal abscess

	<p><u>Very rare</u> BCG infection of implants and surrounding tissue (e.g. aortic graft infection, cardiac defibrillator, hip or knee arthro-plasty), regional lymph node infection, osteomyelitis, bone marrow infection, peritonitis, psoas abscess, infection of the glans penis, orchitis or epididymitis resistant to anti-tuberculosis therapy</p>
Blood and lymphatic system disorders	<p><u>Uncommon</u> Cytopenia, anaemia</p> <p><u>Very rare</u> Cervical lymphadenitis</p> <p><u>Not known</u> Haemophagocytic syndrome</p>
Immune system disorders	<p><u>Very common</u> Transient systemic BCG reaction (fever < 38.5 °C, flu-like symptoms including malaise, fever, chills, general discomfort, myalgia)</p> <p><u>Very rare</u> Hypersensitivity reaction (e.g., oedema of eyelids, cough)</p>
Eye disorders	<p><u>Very rare</u> Chorioretinitis, conjunctivitis, uveitis</p>
Vascular disorders	<p><u>Uncommon</u> Hypotension</p> <p><u>Very rare</u> Vascular fistula</p> <p><u>Not known</u> Vasculitis (including vasculitis of the central nervous system)</p>
Respiratory, thoracic and mediastinal disorders	<p><u>Uncommon</u> Pulmonary granuloma</p>
Gastrointestinal disorders	<p><u>Very common</u> Nausea</p> <p><u>Common</u> Diarrhoea, abdominal pain</p> <p><u>Very rare</u> Vomiting, intestinal fistula</p>
Hepatobiliary disorders	<p><u>Uncommon</u> Hepatitis</p>
Skin and subcutaneous tissue disorders	<p><u>Uncommon</u> Skin rash</p>

Musculoskeletal and connective tissue disorders	<u>Common</u> Myalgia <u>Uncommon</u> Arthritis, arthralgia
Renal and urinary disorders	<u>Very common</u> Frequent urination with discomfort and pain <u>Common</u> Urinary incontinence <u>Uncommon</u> Macroscopic haematuria, bladder retention, urinary tract obstruction, contracted bladder <u>Not known</u> Renal failure, pyelonephritis, nephritis (including tubulointerstitial nephritis, interstitial nephritis and glomerulonephritis)
Reproductive system and breast disorders	<u>Not known</u> Genital disorders (e.g., vaginal pain, dyspareunia), oligospermia, azoospermia
General disorders and administration site conditions	<u>Very common</u> Fatigue <u>Common</u> Fever > 38.5 °C <u>Very rare</u> Peripheral Oedema
Investigations	<u>Uncommon</u> Hepatic enzyme increased <u>Not known</u> Prostatic specific antigen (PSA) increased

Adverse reactions of BCG treatment are frequent but generally mild and transient. Adverse reactions usually increase with the number of BCG instillations.

In common cases myalgia and in uncommon cases, arthritis/arthralgias and skin rash may occur. In most cases of arthritis, arthralgias and skin rash, these can be attributed to hypersensitivity reactions of the patient to BCG. It may be necessary in some cases to discontinue the administration of BCG-medac.

Local adverse reactions

Discomfort and pain when urinating and frequent urination occur in up to 90 % of patients. The cystitis and inflammatory reaction (granulomata) may be an essential part of the anti-tumour activity. Other observed local adverse reactions are macroscopic haematuria, urinary tract infection, bladder retraction, urinary obstruction, bladder contracture, symptomatic granulomatous prostatitis, orchitis and

epididymitis. Renal abscess is rarely observed. Furthermore, genital disorders (e.g., vaginal pain, dyspareunia) may occur with an unknown frequency.

Transient systemic BCG reaction

Low grade fever, flu-like symptoms and general discomfort may occur. These symptoms usually subside within 24 – 48 hours and should be managed by standard symptomatic treatment. These reactions are signs of a starting immune reaction. All patients receiving the medicinal product should be carefully monitored and advised to report all incidences of fever and other events outside the urinary tract.

Severe systemic adverse reactions/infections

Distinguishing a BCG infection from a BCG immune reaction poses a challenge, as the symptoms are very similar at the beginning. In contrast to this, a transient systemic BCG reaction is a very common adverse reaction that must be differentiated.

The clinical signs and symptoms of a BCG infection/reaction at the beginning are fever > 39.5 °C during at least 12 hours, fever > 38.5 °C during at least 48 hours and worsening of general condition.

Typical signs of an infection are the development of miliary pneumonia, granulomatous hepatitis, liver function test abnormalities (especially an elevation in alkaline phosphatase), organic dysfunction (other than genito-urinary tract) with granulomatous inflammation at biopsy over time.

If a systemic BCG infection is suspected, a physician specialised in infectious diseases should be consulted. BCG infection can be potentially fatal.

Although the symptoms of a systemic BCG infection do not differ from tuberculosis, the patient does not need to be isolated, because *Mycobacterium bovis* is less pathogenic for humans than *Mycobacterium tuberculosis*.

In case of flare-up of a latent infection the patients usually present with symptoms of fever and weight loss of unknown origin. Several case reports show that the diagnosis is challenging as the symptoms vary and a causal relationship with BCG infection is not suspected by physicians.

Early diagnosis and appropriate treatment are important for the outcome, especially in elderly or debilitated patients, to avoid fatal consequences.

A physician specialised in infectious diseases should be consulted.

The additional use of corticosteroids is recommended in case of sepsis, granulomatous reactions (e.g. lung or liver) and other immune-mediated reactions.

Treatment recommendations see table below.

Treatment of symptoms, signs and syndrome	
Symptoms, signs or syndrome	Treatment
1) Symptoms of vesical irritation lasting less than 48 hours	Symptomatic treatment
2) Symptoms 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 anti-tuberculosis 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	<p>Discontinue therapy with BCG-medac.</p> <p>Administer isoniazid (INH)* and rifampicin* for 3 to 6 months according to severity.</p> <p>In case of anti-tuberculosis treatment, therapy with BCG-medac should definitively be discontinued.</p>
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	<p>Discontinue therapy with BCG-medac.</p> <p>Consider a consultation with a specialist for infectious diseases.</p> <p>Administer antihistaminic or non-steroidal anti-inflammatory drugs. Cortisone therapy should be considered in case of immune-mediated reactions. If no response, administer isoniazid* for 3 months.</p> <p>In case of anti-tuberculosis treatment, therapy with BCG-medac should definitively be discontinued.</p>
<p>7) Systemic BCG reaction/infection** without septic shock signs</p> <p>** see definition systemic BCG reaction/infection section 4.4</p>	<p>Definitely discontinue therapy with BCG-medac.</p> <p>Consider a consultation with a specialist for infectious diseases.</p> <p>Administer a triple-drug anti-tuberculosis therapy* for 6 months and low dose corticosteroid therapy.</p>
8) Systemic BCG reaction/infection with septic shock signs	<p>Definitely discontinue treatment with BCG-medac. Administer immediately a triple anti-tuberculosis therapy* combined with high-dose, quick-acting corticosteroids.</p> <p>Seek the opinion of a specialist for infectious diseases.</p>

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

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 or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Overdose is unlikely to occur as one vial of BCG-medac corresponds to one dose.

There are no data indicating that an overdose may lead to any other symptoms than the described undesirable effects (see section 4.8).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunostimulants – Other immunostimulants
ATC code: L03AX03

BCG-medac is a lyophilised suspension of live *Bacillus Calmette-Guérin* bacteria with low infectious potential derived from *Mycobacterium bovis*, strain RIVM.

Mechanism of action

BCG-medac stimulates the immune system and has anti-tumour activity. Study data suggest that BCG acts as a non-specific immunopotentiator, not by a single mechanism but by a variety of actions involving cells of the immune system. BCG has a stimulating effect on the spleen, enhances macrophage function in the spleen and activates natural killer cells. BCG instillation stimulates the increase of granulocytes, monocytes/macrophages and T-lymphocytes, indicating local activation of the immune system. Cytokines IL1, IL2, IL6 and TNF α are also increased.

5.2 Pharmacokinetic properties

Most of the bacilli are excreted in the urine in the first hours after the instillation. BCG attachment to the bladder urothelium has been shown to be important for induction of the pharmacological effect at the site of application. There have been single case reports in which BCG bacteria persisted in the urinary tract for more than 16 months (see section 4.4).

5.3 Preclinical safety data

BCG strain RIVM was tested for toxicity, immunostimulatory properties and anti-tumour activity in a variety of animals. High doses of BCG caused weight retardation in mice, and liver disturbance was also observed. Intravenous injection in rabbits appeared to be pyrogenic. Repeated instillations in guinea pigs induced inflammatory reactions in the bladder wall. As unwanted adverse reactions granulomatous lesions in the liver and lung were observed after high doses. Intravesical application in dogs showed minimal mechanical lesions of the urothelium whereas no signs of active inflammation were observed in the sub-urothelial stroma.

No mutagenicity, carcinogenicity and reproduction studies have been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder: polygeline, glucose anhydrous and polysorbate 80.
Solvent: sodium chloride and water for injections.

6.2 Incompatibilities

BCG-medac is incompatible with hypotonic and hypertonic solutions.

6.3 Shelf life

2 years.

After reconstitution the product should be used immediately.

6.4 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).

Do not freeze.

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

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

6.5 Nature and contents of container

Powder in a vial (type I glass) with a rubber stopper + 50 ml of solvent in a bag (PVC) with a vial connector and a catheter adapter (conical or Luer-Lock adapter).

Pack sizes (conical adapter): 1, 3, 5 or 6 with or without catheter(s) connector(s).

Pack sizes (Luer-Lock adapter): 1 or 3 with or without catheter(s).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Instructions for use/handling

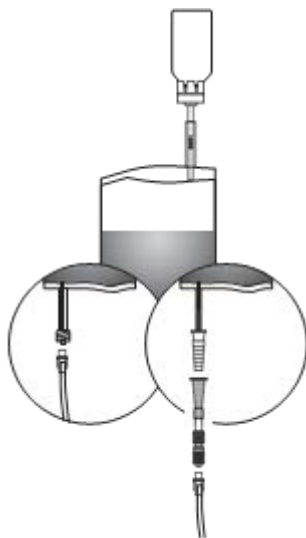
Administration of the catheter should be done carefully to avoid injuries of the epithelium which may lead to development of systemic BCG infection. Use of a lubricant is recommended to minimise the risk of traumatic catheterisation and to reduce patient discomfort. Women might need less lubricant than men. A draining of the bladder after catheterisation reduces residual lubricant before BCG is applied.

Before use the product has to be resuspended under aseptic conditions with sterile 9 mg/ml (0.9 %) sodium chloride solution (see below). Remix the suspension before use by rotating gently. Avoid skin contact with BCG-medac. The use of gloves is recommended.

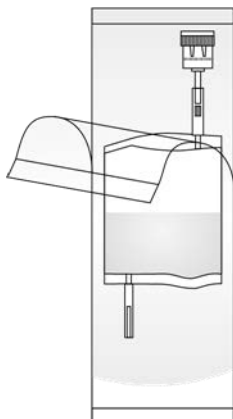
Visible macroscopic particles do not affect the efficacy and safety of the medicinal product.

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

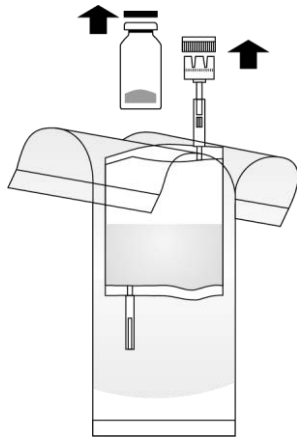
The following handling instructions apply to the system with conical or Luer-Lock adapter.



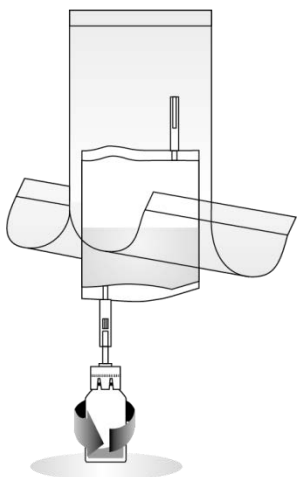
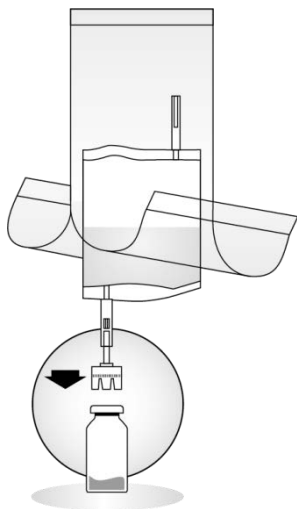
1. Tear open the protective bag, but do not remove it completely! This will protect the tip of the instillation system from contamination up to the last minute.



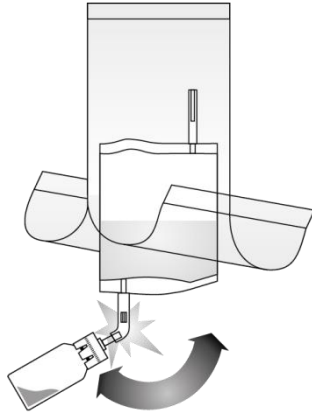
2. Remove the caps from the vial and instillation system. Lay out a disposal bag.



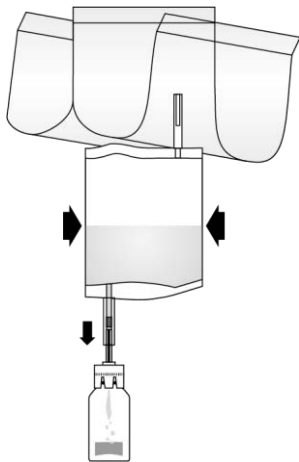
3. Place the BCG-medac vial on a solid surface (e.g., table) and press the vial connector of the instillation system upright and firmly onto the BCG-medac vial. Turn the vial 2 times completely in the same direction.



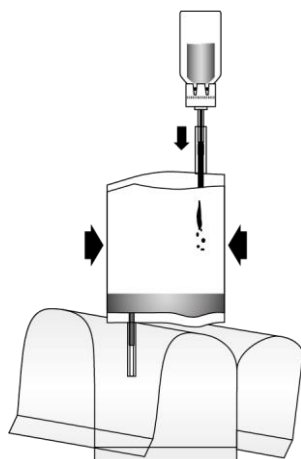
4. Break open the mechanism in the tube of the vial connector by repeated bending backwards and forwards. This establishes the connection. Please hold the tube – and not the vial – during this process!



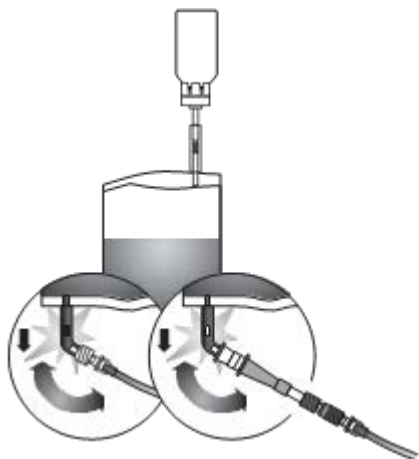
5. Pump the liquid into the vial, but do not fill the vial completely. If flow is not possible, turn the vial again 2 – 3 times in both directions to assure that the septum is completely penetrated. Repeat this step until flow is possible.



6. Invert the entire system. Pump air from the instillation system into the vial at the top and draw the reconstituted BCG-medac into the instillation system. Do not remove the vial.



7. Keep the instillation system in an upright position. Now remove the protective bag completely. Connect the catheter (and a connector [conical to Luer-Lock]) to the instillation system. Now break the sealing mechanism in the tube section by bending it back and forth and instil the BCG-medac suspension into the patient's bladder. At the end of the instillation free the catheter by pressing air through. Keep the instillation system squeezed and place it together with the catheter into the disposal bag.



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

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 11587/0139

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

06/09/2023

10 DATE OF REVISION OF THE TEXT

05/2024