

Version 4.2, 04/2021

PACKAGE LEAFLET

Package leaflet: Information for the user

Vesiculture 30 mg/vial

Powder for intravesical suspension

Mycobacterium bovis BCG (Bacillus Calmette-Guérin), Danish strain 1331, live attenuated.

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 nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Vesiculture is and what it is used for
2. What you need to know before you are treated with Vesiculture
3. How to be treated with Vesiculture
4. Possible side effects
5. How to store Vesiculture
6. Contents of the pack and other information

1. What Vesiculture is and what it is used for

Vesiculture contains live attenuated tuberculosis bacteria which stimulate the immune defence without causing disease. Vesiculture stimulates the immune defence in the bladder to counteract tumours. Vesiculture is used for treatment of tumours in the bladder.

2. What you need to know before you are treated with Vesiculture

Do not be treated with Vesiculture

- if you are allergic to the active substance in Vesiculture or any of the other ingredients of this medicine listed in section 6.
- if you have a weakened immune system due to
 - o disease such as leukaemia or HIV infection.
 - o certain therapy such as radiation.
 - o medications such as systemic cytostatic medicinal products or medicinal products that decrease the immune response.
- if you have signs of active tuberculosis. A test for tuberculosis is recommended before beginning the treatment.
- if you are treated with anti-tuberculosis medication (e.g. isoniazid, rifampicin, streptomycin and ethambutol).
- if you are pregnant or breast-feeding.
- if you have been treated with radiotherapy of the bladder.
- If you suffer from an acute infection of the urinary tract.
- If you have bladder perforation.

Warnings and precautions

Vesiculture shall only be used for instillation in the bladder.

Talk to your doctor or nurse before being treated with Vesiculture. The doctor will be particularly cautious about treating you with Vesiculture in the following situations:

- if you have an infection of the bladder or urinary tract. Terminate the treatment with Vesiculture until you have a negative urine test and treatment with antibiotics has been ceased.

- if you have visible blood in your urine or any other signs of damage in the urinary tract.

Be aware of the following:

- infection of implants and transplants can occur after treatment with Vesiculture.
- joint pain and swelling may occur, especially in patients with tissue type HLA-B27.
- it is recommended that you wash hands and genital area after urinating, especially the first time after you have been treated with Vesiculture.
- while you are in treatment with Vesiculture you should avoid contact with individuals whose immune system is weakened, such as:
 - o individuals infected with HIV.
 - o individuals who receive chemotherapy or radiotherapy
- in order to protect your partner, you should avoid intercourse or use a condom during intercourse for the first week after bladder irrigation.

Children and adolescents

Vesiculture is not recommended in this age group.

Other medicines and Vesiculture

Tell your doctor if you are taking, have recently taken or might take any other medicines.

Talk to your doctor if you are taking any of the following medicines, as they may affect the therapeutic effect of Vesiculture:

- antibiotics (medicine for treatment of bacterial infections).
- immunosuppressants (medicine that inhibits the immune response).
- bone marrow suppressants (medicine that inhibits the bone marrow).
- radiation therapy.

These types of medicines and treatments can affect your immune response and is not recommended while you are treated with Vesiculture.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before you are treated with Vesiculture.

Pregnancy

Do not be treated with Vesiculture if you are pregnant.

Breast-feeding

Do not breast-feed if you are being treated with Vesiculture.

Driving and using machines

Vesiculture may cause side effects that can affect the ability to use machines or drive safely in traffic to a greater or lesser extent. You should therefore be aware of how the medicine affects you.

3. How to be treated with Vesiculture

Your doctor can tell you which dose you receive and how often you will receive it. Ask your doctor if you are uncertain about this.

Your doctor or nurse will administer the product into the bladder with the contents of 4 vials, reconstituted in sterile sodium chloride 9 mg/mL (0.9%), solution for injection, preservative-free. You should empty your bladder prior to the treatment. You should not drink from four hours before until two hours after treatment. The suspension should work for two hours if possible. You should therefore try to retain the urine for two hours. To ensure that Vesiculture is in adequate contact with the entire surface of the bladder mucosa, it is recommended that you move lightly. You should empty the bladder in a sitting position after two hours.

You should normally be treated once a week for six weeks. Your doctor may decide to recommend continuation of the treatment.

Treatment normally begins at least 2 weeks after an operation on the bladder.

If your treatment with Vesiculture is terminated

If your treatment is interrupted, temporarily or otherwise, your doctor will inform you.

If you have any further questions, ask your doctor or healthcare professional.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Contact your doctor or emergency ward if you experience any of the below mentioned **serious side effects** after treatment:

Very rare: may affect up to 1 in 10,000 people.

- Infection with Bacillus Calmette-Guérin (BCG). If the bladder is accidentally injured during treatment with Vesiculture or it is administered into a muscle or vein this can result in a severe infection with BCG.

Possible symptoms are:

- general malaise with fever and coughing for 24 –48 hours.
- weight loss due to pneumonia caused by the BCG bacteria.
- jaundice due to hepatitis.
- paleness and fatigue due to anaemia. These reactions may develop after the treatment has ceased.

Not known: frequency cannot be estimated from the available data

- Delayed BCG-infection:
In single cases BCG-bacteria may remain in the body for years and cause delayed symptoms and signs, even years after the last dose of BCG has been administered. Signs of inflammation could be similar to a severe BCG-infection like mentioned in the section above (e.i. Infection with Bacillus Calmette-Guérin) . Talk to your doctor, if any unexpected symptoms arise.

Non-serious side effects

Very common: may affect more than 1 in 10 people.

- Frequent urination of limited amount.
- Sudden urge to urinate.
- Blood in the urine.
- Painful and frequent urination due to urinary tract infection.
- Urinary tract infection.
- Nausea.
- Influenza-like symptoms with low to moderate fever, malaise, muscle pain.

Common: may affect up to 1 in 10 people.

- Inflammation of the bladder mucosa.
- Cutaneous rash.
- Joint inflammation, joint pain.
- Fever over 39°C.
- Fever, pain and red and swollen scrotum, swelling and tenderness of the bitesticles due to inflammation of the bitesticles.

Rare: may affect up to 1 in 1,000 people.

- Problems with urination due to temporary narrowing of the urethra.

- Fever, swelling, pain and tenderness in the scrotum due to inflammation of the testicles.
- Discharge from the urethra, pain behind the pubic bone, stinging during urination due to inflammation of the prostate.

Very rare: may affect up to 1 in 10,000 people.

- Low volume, frequent urination due to bladder contraction.

Reporting of side effects

If you get any side effects, talk to your doctor 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 Vesiculture

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

Do not use Vesiculture after the expiry date which is stated on the carton. The expiry date is the last day of the month.

Store in a refrigerator (2°C – 8°C).

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

6. Contents of the pack and other information

What Vesiculture contains

- The active substance is a freeze-dried powder, which contains live attenuated bacteria of the type *Mycobacterium bovis* BCG (Bacillus Calmette-Guerin), Danish strain 1331, 30 mg per vial.
- The other excipient is monosodium glutamate.

What Vesiculture looks like and contents of the pack

Vesiculture is a powder for intravesical suspension supplied in vials of 30 mg.

Pack size: 4 x 30 mg.

Marketing Authorisation Holder and Manufacturer

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This medicine is authorised in the Member States of the European Economic Area under the following names:

DK, DE, EL, ES, FI, IT: VesiCulture

AT: VesiCulture, 30 mg/durchstechflasche, Pulver zur Herstellung einer Suspension zur intravesikalen Anwendung

IE, SE: Vesiculture

HU: Vesiculture 30 mg por intravezikális szuszpenzióhoz

FR: Veleris, 30 mg, Poudre pour suspension intravésicale
SI: Veleris

This leaflet was last revised in November 2025

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The following information is intended for healthcare professionals only:

Special warnings and precautions for use

Treatment with Vesiculture should only be carried out by doctors with special expertise in malignant illnesses in the bladder and their treatment.

Vesiculture shall only be used for instillation in the bladder and must not be used for subcutaneous, intradermal, intramuscular or intravenous administration or for BCG vaccination.

- Damage to the urethra or mucous membrane of the bladder (e.g. triggered by traumatic catheterization) may result in macroscopic haematuria. Treatment with Vesiculture is contraindicated in such cases as BCG infection and sepsis can develop. The treatment should be postponed until the mucous membranes have healed and haematuria has resolved.
- Urinary tract infection should be ruled out before each instillation, since inflammation of the mucous membranes of the bladder can increase the risk of haematological spread of BCG. If a urinary tract infection appears during the course of treatment, treatment should be discontinued until a negative urine culture is achieved, and an eventual treatment with antibiotics has been discontinued.
- Patients should be monitored for presence of symptoms of systemic BCG infection after each bladder irrigation. The risk of systemic infection is higher in elderly patients and patients with hepatic and renal impairment. This should be considered before treatment with Vesiculture.
- Infection of implants and transplants has been reported after treatment with BCG bladder irrigation in patients with e.g. aneurysm or prosthesis.
- In case of a suspicion of a systemic infection a physician specialised in infectious diseases should be consulted. BCG-infection can potentially be fatal.
- Isolated cases of BCG persisting in the body for several years have been reported. These latent BCG infections can reappear years after the initial infection and can lead to granulomatous pneumonia, abscesses, infected aneurysms, and infection of an implant, graft, or surrounding tissue. Patients should be warned of the possibility of late reactivation of latent BCG infection and advised on what to do if symptoms such as fever and unexplained weight loss occur. If reactivation of latent BCG infection is suspected, a physician specializing in infectious diseases should be consulted.
- BCG Danish strain 1331 is completely sensitive to streptomycin, rifampicin and ethambutol. The strain can be considered to have intermediate sensitivity to isoniazid and is resistant to pyrazinamide.
- Vesiculture should not be handled in the same room or by the same healthcare professionals preparing cytostatics.
- Vesiculture should not be handled by individuals affected by known immunodeficiencies.
- If a Closed System Transfer Device (CSTD) is not applied, see *Handling*, the reconstitution of the suspension for bladder irrigation should be performed under aseptic conditions.
- Self-inoculation of BCG can occur through open wounds, inhalation or ingestion of Vesiculture. Exposure to BCG is not expected to have health consequences for healthy individuals. However, in case of suspected self-inoculation, it is recommended to perform a Mantoux test immediately after exposure and after 6 weeks.
- Contact to skin or mucosa with Vesiculture should be avoided. Contamination can lead to a hypersensitivity reaction. Use appropriate skin disinfectant in case of contamination of skin lesions.
- Spillage of Vesiculture can cause BCG contamination. Therefore, spilled product must be covered with paper wetted with hospital disinfectant or 10% chloramine solution for at least 10 minutes. All waste materials must be disposed of as potentially contagious waste.

- It is recommended to wash hands and genital area after micturition, especially after the first micturition following BCG instillation.
- Instillation of Vesiculture may sensitise patients to tuberculin after 6-8 weeks, resulting in a positive Mantoux test. Therefore, reactivity to tuberculin should be measured before administration of Vesiculture.
- The risk of bladder contraction may increase in patients with low bladder capacity.
- In patients with tissue type HLA-B27 the occurrence of reactive arthritis or Reiter's syndrome may be increased. Patients treated with Vesiculture should avoid contact with immunocompromised individuals.
- In order to protect against possible BCG transmission, the patient should be recommended to avoid intercourse or use a condom during intercourse in the first week after bladder irrigation.

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Handling

Vesiculture is to be dissolved in sterile sodium chloride 9 mg/mL (0.9%) solution for injection, preservative-free, before use, and must not be mixed with other medicinal products.

Vesiculture contains live, attenuated mycobacteria, and proper attention to avoid bacterial transmission should be exercised. Reconstitution should be carried out under aseptic conditions.

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

Instructions for preparation of reconstituted product

For intravesical instillation 4 vials of Vesiculture is resuspended in 50 mL sterile sodium chloride 9 mg/mL (0.9%) solution for injection, preservative-free, as follows:

1. Using a sterile syringe, transfer approximately 2-3 mL sterile sodium chloride 9 mg/mL (0.9%) solution for injection, preservative-free, to each of the 4 vials. If alcohol swabs are used for disinfection of the rubber stopper, the surface of the stopper must be completely dry before penetrating with the syringe.
2. Resuspend the content of each vial by carefully inverting it a few times, then swirl gently. DO NOT SHAKE.
3. Transfer the contents of the 4 vials to one single 50 mL syringe.
4. Draw additional sterile sodium chloride 9 mg/mL (0.9%) solution for injection, preservative-free, into the syringe until the total volume is 50 mL.

The suspension in the 50 mL syringe should be homogeneous, and slightly cloudy. The product should be used as soon as possible after reconstitution and within 4 hours. Avoid unnecessary exposure to light.

At the time of administration, the suspension should be swirled gently to homogenise.

A Closed System Transfer Device (CSTD) may be considered when reconstituting and transferring Vesiculture to the instillation equipment. Please refer to the instructions for use provided with the CSTD for a full description of the product reconstitution using CSTD.

Method of administration

Vesiculture shall be administered by intravesical instillation.

A urethral catheter is inserted into the bladder under aseptic conditions. A sufficient quantity of lubricant should be used to avoid traumatising the urinary mucosa and to reduce the discomfort for the patient associated with the procedure. The bladder must be emptied before BCG instillation and the patient should not drink from 4 hours before the instillation and until 2 hours after the instillation. Complete draining of the bladder after catheterisation reduces residual lubricant which may have reached the bladder before Vesiculture is instilled.

The suspension is slowly instilled into the empty bladder by means of the catheter, taking care not to force the flow. The catheter is removed once instillation is complete, and the patient is instructed to retain the suspension in the bladder for 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 not be immobilised. If bedridden, the 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.

Overdose

The risk of BCG infection may increase in the event of an overdose. If an overdose takes place, the patient should be observed for symptoms of systemic BCG infection and, if necessary, treated with anti-tuberculosis medicines.