PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS REGULATIONS (PREPARATIONS) 1986

This medicine is marketed upon physician's prescription only

OncoTICE®

Powder for solution for instillation

Each vial contains:
2-8 x 10^8 CFU Tice BCG.
For a list of inactive ingredients see section 6.1 "What **OncoTICE** contains?". See also section 2.7 "Important information about some of the ingredients of **OncoTICE**".

Read all of this leaflet carefully before you start using this medicine.

- This leaflet contains concise information about the medicine. If you have any further questions, refer to the doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their medical condition seems similar to yours.

WARNING

OncoTICE contains live, attenuated mycobacteria. Because of the potential risk for transmission, prepare, handle, and dispose of OncoTICE as a biohazard material.

BCG infections have been reported in health care workers, primarily from exposures resulting from accidental needle sticks or skin lacerations during the preparation of BCG for administration. Nosocomial infections have been reported in patients receiving parenteral drugs that were prepared in areas in which BCG was reconstituted. BCG is capable of dissemination when administered by the intravesical route, and serious infections, including fatal infections, have been reported in patients receiving intravesical BCG.

1. WHAT ONCOTICE IS INTENDED FOR?

OncoTICE is used to:

- treat bladder cancer
- prevent bladder cancer from coming back after bladder surgery

Therapeutic group: immunostimulating agent

2. BEFORE USING OncoTICE

2.1 Do not use OncoTICE if:

- You are sensitive (allergic) to the active substance (Tice BCG) or any of the other ingredients that this medicine contains. For a list of inactive ingredients, see section 6.1 "What **OncoTICE** contains?".
- You have a urinary tract infection (UTI) or cystitis (inflammation of the bladder). This must be treated first.
- You have blood in your urine.

- You have or think you have tuberculosis. Before you have **OncoTICE**, your healthcare provider may do a skin reaction test, to see if you have tuberculosis. This is called a Tuberculin Test. If you have had **OncoTICE** before, this may give you a positive result in this test.
- You are HIV-positive. You may need to have a blood test for HIV.
- Are pregnant or breast-feeding.

Tell your healthcare provider if any of the following apply to you:
- you have been a drug user and have shared a needle.
- you have had unsafe sex.
- you have had a blood transfusion.
- you have problems with your immune system. This could be something which runs in the family or is caused by an illness or other medicines you are taking.

Do not have **OncoTICE** if any of the above apply to you. If you are not sure, talk to your healthcare provider before being given **OncoTICE**.

2.2 Special warnings regarding use of OncoTICE

Check with your healthcare provider before being given the medicine if:
- Your bladder wall or the tube that goes into your bladder from your kidneys (called the ureter) have been damaged during previous treatment. Treatment with **OncoTICE** will not be given until this has healed.

If you are not sure if any of the above apply to you talk to your healthcare provider before being given **OncoTICE**.

2.3 Interactions with other medicines

If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Especially if you are taking:
- Medicines for tuberculosis - do not have **OncoTICE** and talk to your healthcare provider straight away.
- Antibiotics; medicines which affect the immune system (immuno-suppressants); medicines which affect the production of bone marrow cells (bone marrow suppressants); radiation treatment- these can lower the effect of **OncoTICE**. If you are having any of these medicines or are having radiation treatment, your healthcare provider will probably delay giving you **OncoTICE**.

2.4 Using OncoTICE with food and drink
- Do not drink any liquid for 4 hours **before** you are given **OncoTICE**.
- Do not drink any liquid for 2 hours **after** you have been given **OncoTICE**.

2.5 Pregnancy and breast-feeding

Do not have **OncoTICE** if you are pregnant or breast-feeding. Ask your doctor or pharmacist for advice before taking any medicine if you are pregnant or breast-feeding.

2.6 Driving and using machines

OncoTICE will not affect your being able to drive or use any tools or machines.

2.7 Important information about some of the ingredients of OncoTICE
- **OncoTICE** contains lactose (a type of sugar). If you have been told by your healthcare provider that you cannot tolerate or digest some sugars, talk to your healthcare provider before being given this medicine.
- This medicine contains a very small amount of potassium (less than 1mmol or 39 mg per dose). This means it is essentially ‘potassium-free’.

3. HOW OncoTICE IS GIVEN?

Dosage is according to doctor's instructions only.
Treatment usually includes one instillation a week for 6 weeks. Afterwards, one instillation a week for 3 weeks at months 3, 6 and 12 after initiation of **OncoTICE** treatment. If necessary treatment can be repeated every 6 months with one instillation a week for 3 weeks.

Do not exceed the recommended dose.

Attention: Do not swallow! This medicine is intended for instillation into the urinary bladder only.

Directions for use:
Before it is given

- Do not drink any liquid the 4 hours before **OncoTICE** is given to you.
- You will be asked to urinate immediately before **OncoTICE** is given to you.

Being given your medicine

- First your genital area will be cleaned with a sterile solution.
- A healthcare provider will then pass a small flexible tube into your bladder. This will remove any urine that is still in your bladder.
- **OncoTICE** is then run into your bladder through this tube. This will only take a few minutes.
- The tube will then be removed.

After it has been given

- **OncoTICE** will be left in your bladder for 2 hours.
- During this time you should move around a little. This makes sure that the **OncoTICE** is spread around your entire bladder wall.
- Do not drink any liquid for 2 hours after you have been given **OncoTICE**.
- After 2 hours you will be asked to urinate, to empty your bladder. You should do this while sitting down to avoid splashing your urine around the toilet.

During the next 6 hours

- If you need to urinate again, also do this while sitting down.
- Every time you urinate, add two cups of household bleach to the toilet.
- Leave the bleach and urine to stand in the toilet for 15 minutes before flushing.

Having sex in the week after having Oncotice
If you have sexual intercourse during the week after being given the medicine, you must use a condom. This will lower the chance of the BCG bacteria being passed to your partner.

If you have more Oncotice than you should
OncoTICE is made up from a standard bottle by your healthcare provider. It is unlikely that you will receive too much **OncoTICE**. If you do have too much, your healthcare provider will check carefully to see whether you have BCG infection. If necessary you will need to have treatment for tuberculosis.

If you or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or to a hospital emergency room and bring the package of the medicine with you.

Treatment should be completed as recommended by the doctor.
Even if there is an improvement in your health, do not discontinue use of this medicine before consulting your doctor.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take a medicine. Wear glasses if you need them.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, **OncoTICE** may cause side effects in some users. Do not be alarmed by reading the list of side effects, you may not suffer from any of them.

If you notice the following side effects, see your doctor straight away:

- a high temperature (fever) above 39°C that lasts for more than 12 hours, even after taking medicines like paracetamol to lower your temperature.
- signs of a BCG or tuberculosis infection:
- cough or bronchitis
- chest pain or shortness of breath
- sweating
- sore throat
- runny nose
- swelling of your lymph glands.

See your doctor straight away if you notice any of these side effects.

The following side effects have been reported but the frequency cannot be estimated from the available information (frequency not known):

- allergic reactions that can range from mild to severe. Symptoms may include rash, itching, or more severe skin reactions.
- BCG infection in the blood (sepsis). Severe condition with multiple symptoms that may include fever, malaise, chills, sweats, weight loss and shortness of breath.
- abnormal arterial dilation for bacterial infection (infective aneurysm). Severe condition with symptoms that may include abdominal and/or back pain and fever.
- inflammation of the blood vessels. Severe condition with multiple symptoms that may include fever, headache, fatigue, weight loss, and general aches and pains.
- a serious and potentially life-threatening condition where the immune system becomes overactive and produces too many infection fighting cells, which can cause inflammation and damage to body's own tissues and organs (hemophagocytic lymphohistiocytosis). Symptoms may include fever that doesn't go away, feeling very tired or weak, looking pale, feeling lightheaded or short of breath, or easy bruising.

Other side effects include:

Very common (affects more than 1 in 10 people)

- bladder inflammation, pain when urinating, having to urinate often, and bloody urine. Usually these go away within two days.
- flu-like symptoms such as fever, fatigue and feeling off-colour and tired (malaise). These usually happen about 4 hours after treatment and lasts for 24 to 48 hours.

Common (affects less than 1 in 10 people)

- painful joints or arthritis
- muscle pain or stiffness
- nausea and vomiting
- abdominal pain or diarrhoea
- anaemia
- problems urinating
- shivering with a high temperature (fever)
- lung inflammation
- urinary tract infection
- urge to urinate

- abnormal urine lab test

Uncommon (affects less than 1 in 100 people)

- skin rash
- jaundice (yellow colour of your skin or eyes)
- pus in your urine
- difficulty urinating
- decreased amount of red blood cells or platelets possibly associated with symptoms such as fatigue and/or bruises
- decrease of white blood cells
- abnormal liver function test
- bladder constriction and blocked urine flow
- tuberculosis infections

Rare (affects less than 1 in every 1,000 people)

- inflammation of the epididymis (tube at the back of the testicles)
- cough

Very Rare (affects less than 1 in every 10,000 people)

- headache
- back pain
- increased muscle tension
- swollen legs or arms
- low blood pressure
- flatulence or discomfort following meals
- loss of appetite or weight loss
- hair loss
- prickling, burning, pins and needles or itching skin
- eye infection
- feeling confused, sleepy or dizziness (spinning sensation)
- kidney problems
- increased perspiration
- bronchitis
- shortness of breath
- sore throat
- runny nose
- swelling of the lymph glands
- granuloma (nodule in an organ)
- inflammation of the glans
- inflammation of the testicles
- inflammation of the prostate
- Reiter's syndrome (inflammation of the eyes, joints and genitourinary system)
- Lupus vulgaris (tuberculosis of the skin)
- elevation of Prostatic specific antigen (PSA) (prostate laboratory test)
- burning, itching and soreness in the female genital area
- chest pain

If a side effect appears, if any of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, contact your doctor immediately.

Side effects can be reported to the Ministry of Health by using the link "Adverse Drug Reactions Report" at the home page of the Ministry of Health's web site (www.health.gov.il) which refers to the online side effects reporting form, or by using the link: https://sideeffects.health.gov.il

5. HOW TO STORE OncoTICE?

- Avoid Poisoning! This medicine and any other medicine must be stored in a safe place out of the reach and sight of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- **OncoTICE** will be stored in the hospital according to the instructions given by the manufacturer on the packaging.
- Do not use the medicine after the expiry date (exp. date) which is stated on the pack. The expiry date refers to the last day of the indicated month.
- **Storage conditions**:
  Store at 2-8ºC, protect from light.
- Medicines should not be disposed of via wastewater or household waste. Ask the pharmacist how to dispose of medicines you no longer use. These measures will help to protect the environment.

6. FURTHER INFORMATION

6.1 What OncoTICE contains?

In addition to the active ingredient, **OncoTICE** also contains:
Lactose monohydrate, Asparagine monohydrate, citric acid monohydrate, potassium phosphate (dibasic), magnesium sulfatesulfate heptahydrate, iron ammonium citrate, glycerin, zinc formate, ammonium hydroxide

6.2 What OncoTICE looks like and contents of the pack

OncoTICE is a white to off-white cake or powder, packed in 2 ml glass vial (packs of 1 or 3 vials).
Not all pack sizes are marketed.

6.3 Marketing authorization holder and Importer

Merck Sharp & Dohme (Israel-1996) Company Ltd., 34 Ha'charash St., Hod-Hasharon.

Revised in February 2026.
Drug registration no. listed in the official registry of the Ministry of Health: 103-18-28561

Instructions for healthcare professionals

OncoTICE contains live, attenuated mycobacteria. Because of the potential risk for transmission, it should be prepared, handled and disposed of as a biohazard material.

Perform the following procedures under aseptic conditions using sterile physiological saline solution as the diluent and suitable techniques to ensure protection of the health care worker.

The use of closed-system transfer device products may be considered when transferring **OncoTICE** from primary packaging to instillation equipment.

Reconstitution

Transfer 50ml of the diluent into a sterile container and add 1ml from the sterile container to the vial. Ensure that the needle is inserted through the center of the rubber stopper. Allow to stand for a few

minutes then gently swirl until a homogenous suspension is obtained. Forceful agitation should be avoided.

Preparation of the solution for instillation

Transfer the reconstituted contents of the vial back into the container. Rinse the vial by transferring 1ml from the container back into the vial, then add back to the container. If a closed-system transfer device is not available, dilute the reconstituted 1ml suspension in sterile physiological saline up to a volume of 49ml. Then rinse the empty vial with 1ml of sterile physiological saline. Add the rinse fluid to the reconstituted suspension for a final volume of 50ml.

Mix the suspension carefully.

The suspension, with a total volume of 50ml is now ready for instillation; it contains a total of 2-8 x 10^8 CFU of Tice BCG.