TICE BCG- bacillus calmette-guerin powder, for suspension
Merck Sharp & Dohme LLC

TICE® BCG
BCG Live
For Intravesical Use

WARNING

TICE® BCG contains live, attenuated mycobacteria. Because of the potential risk for transmission, prepare, handle, and dispose of TICE® BCG as a biohazard material (see PRECAUTIONS and DOSAGE AND ADMINISTRATION sections).

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 (see WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS sections).

DESCRIPTION

TICE® BCG (BCG LIVE) for intravesical use, is an attenuated, live culture preparation of the Bacillus of Calmette and Guerin (BCG) strain of *Mycobacterium bovis.*[1] The TICE® seed lot used in this TICE® BCG preparation was developed at the University of Illinois from two BCG strains originated at the Pasteur Institute.

The medium in which the BCG organism is grown for preparation of the freeze-dried cake is composed of the following ingredients: glycerin, asparagine, citric acid, potassium phosphate, magnesium sulfate, and iron ammonium citrate. The final preparation prior to freeze drying also contains lactose.

The freeze-dried BCG preparation is delivered in glass vials, each containing 1 to 8×10^8 colony forming units (CFU) of TICE BCG which is equivalent to approximately 50 mg wet weight. Determination of *in vitro* potency is achieved through colony counts derived from a serial dilution assay. A single dose consists of 1 reconstituted vial (see **DOSAGE AND ADMINISTRATION**).

For intravesical use the entire vial is reconstituted with sterile saline. TICE BCG is viable upon reconstitution.

No preservatives have been added.

CLINICAL PHARMACOLOGY

TICE® BCG induces a granulomatous reaction at the local site of administration. Intravesical TICE BCG has been used as a therapy for, and prophylaxis against, recurrent tumors in patients with carcinoma *in situ* (CIS) of the urinary bladder, and to prevent recurrence of Stage TaT1 papillary tumors of the bladder at high risk of recurrence. The precise mechanism of action is unknown.

CLINICAL STUDIES

Carcinoma *in situ* (Bladder Cancer)

To evaluate the efficacy of intravesical administration of TICE® BCG in the treatment of carcinoma *in situ*, patients were identified who had been treated with TICE BCG under 6 different Investigational New Drug (IND) applications in which the most important shared aspect was the use of an induction plus maintenance schedule. Patients received TICE BCG (50 mg; 1 to 8 x 10^8 CFU) intravesically, once weekly for at least 6 weeks and once monthly thereafter for up to 12 months. A longer maintenance was given in some cases.

The study population consisted of 153 patients, 132 males, 19 females, and 2 unidentified as to gender. Thirty patients lacking baseline documentation of CIS and 4 patients lost to follow-up were not evaluable for treatment response. Therefore, 119 patients were available for efficacy evaluation. The mean age was 69 years (range: 38–97 years).

There were 2 categories of clinical response: (1) Complete Histological Response (CR), defined as complete resolution of carcinoma *in situ* documented by cystoscopy and cytology, with or without biopsy; and (2) Complete Clinical Response Without Cytology (CRNC), defined as an apparent complete disappearance of tumor upon cystoscopy. The results of a 1987 analysis of the evaluable patients are shown in **Table 1**.

Table 1: The Response of Patients With CIS Bladder Cancer in 6 IND Studies

	Entered	Evaluable	CR	CRNC	Overall response
No. (%) of patients	153	119 (78%)	54 (46%)	36 (30%)	90 (76%)

A 1989 update of these data is presented in **Table 2**. The median duration of follow-up was 47 months.

Table 2: Follow-up Response of Patients With CIS Bladder Cancer in 6 IND Studies

	1989 Status of 90 Responders (CR or CRNC)			
Response	1987/CR n=54	1987/CRNC n=36	1987 Response n=90	Percent
CR	30	15	45	50
CRNC	0	0	0	0
Unrelated deaths	6	6	12	13

Failure	18	15	33	37

There was no significant difference in response rates between patients with or without prior intravesical chemotherapy. The median duration of response, calculated from the Kaplan-Meier curve as median time to recurrence, is estimated at 4 years or greater. The incidence of cystectomy for 90 patients who achieved a complete response (CR or CRNC) was 11%. The median time to cystectomy in patients who achieved a complete response (CR or CRNC) exceeded 74 months.

TaT1 Bladder Cancer

The efficacy of intravesical TICE BCG in preventing the recurrence of a TaT1 bladder cancer after complete transurethral resection of all papillary tumors was evaluated in 2 open-label, randomized phase III clinical trials. Initial diagnosis of patients included in the studies was determined by cystoscopic biopsies. One was conducted by the Southwestern Oncology Group (SWOG) in patients at high risk of recurrence. High risk was defined as 2 occurrences of tumor within 56 weeks, any stage T1 tumor, or 3 or more tumors presenting simultaneously. The second study was conducted at the Nijmegen University Hospital; Nijmegen, The Netherlands. In this study patients were not selected for high risk of recurrence. In both studies treatment was initiated between 1 and 2 weeks after transurethral resection (TUR).

SWOG Trial (study 8795)

In the SWOG trial (study 8795) patients were randomized to TICE BCG or mitomycin C (MMC). Both drugs were given intravesically weekly for 6 weeks, at 8 and 12 weeks, and then monthly for a total treatment duration of 1 year. Cystoscopy and urinary cytology were performed every 3 months for 2 years. Patients with progressive disease or residual or recurrent disease at or after the 6 month follow-up were removed from the study and were classified as treatment failures.

A total of 469 patients was entered into the study: 237 to the TICE BCG arm and 232 to the MMC arm. Twenty-two patients were subsequently found to be ineligible, and 66 patients had concurrent CIS, and were analyzed separately. Four patients were lost to follow-up, leaving 191 evaluable patients in the TICE BCG arm and 186 in the MMC arm. Of the patients, 84% were male and 16% were female. The average age of these patients was 65 years old.

The Kaplan-Meier estimates of 2-year disease-free survival are shown in **Table 3**. The difference in disease-free survival time between the 2 groups was statistically significant by the log rank test (P=0.03). The 95% confidence interval of the difference in 2-year disease-free survival was 12% ± 10%. No statistically significant differences between the groups were noted in time to tumor progression, tumor invasion, or overall survival.

Table 3: Results of SWOG Study 8795

	TICE BCG Arm N=191	**MMC Arm N=186**
Estimated disease-free survival at 2 years	57%	45%
95% Confidence Interval (CI)	(50%, 65%)	(38%, 53%)

Nijmegen Study

In the Nijmegen study, the efficacy of 3 treatments was compared: TICE substrain BCG, *Rijksinstituut voor Volksgezondheid en Milieuhygiene* substrain BCG (BCG-RIVM), and MMC.

TICE BCG and BCG-RIVM were given intravesically weekly for 6 weeks. In contrast to the SWOG study, maintenance BCG was not given. Mitomycin C was given intravesically weekly for 4 weeks and then monthly for a total duration of treatment of 6 months. Cystoscopy and urinary cytology were performed every 3 months until recurrence.

A total of 469 patients was enrolled and randomized. Thirty-two patients were not evaluable, 17 were ineligible, 15 were withdrawn before treatment, and 50 had concurrent CIS and were analyzed separately, leaving 387 evaluable patients: 117 in the TICE BCG arm, 134 in the BCG-RIVM arm, and 136 in the MMC arm. Twenty-eight patients (24%) in the TICE BCG arm, 32 patients (24%) in the BCG-RIVM arm, and 24 patients (18%) in the MMC arm had TaG1 tumors. The median duration of follow-up was 22 months (range: 3–54 months).

The Kaplan-Meier estimates of 2-year disease-free survival are shown in **Table 4**. The differences in disease-free survival among the 3 arms were not statistically significant by the log-rank test (P=0.08).

Table 4: Results of Nijmegen Study

	TICE BCG Arm N=117	**BCG-RIVM Arm N=134**	**MMC Arm N=136**
Estimated disease-free survival at 2 years	53%	62%	64%
95% Confidence Interval (CI)	(44%, 64%)	(53%, 72%)	(55%, 74%)

In both the SWOG 8795 study and the Nijmegen study, acute toxicity was more common, and usually more severe, with TICE BCG than with MMC (see **ADVERSE REACTIONS**).

INDICATIONS AND USAGE

TICE® BCG is indicated for:

- the treatment and prophylaxis of carcinoma *in situ* (CIS) of the urinary bladder
- the prophylaxis of primary or recurrent stage Ta and/or T1 papillary tumors following transurethral resection (TUR)

Limitations of Use:

- TICE BCG is not recommended for stage TaG1 papillary tumors, unless they are judged to be at high risk of tumor recurrence.
- ***TICE BCG is not indicated for papillary tumors of stages higher than T1.***

CONTRAINDICATIONS

Immunosuppressed Patients

TICE® BCG should not be used in immunosuppressed patients with congenital or acquired immune deficiencies, whether due to concurrent disease (e.g., AIDS, leukemia, lymphoma) cancer therapy (e.g., cytotoxic drugs, radiation), or immunosuppressive therapy (e.g., corticosteroids).

Patients with Increased Risk of BCG Infection

Treatment should be postponed until resolution of a concurrent febrile illness, urinary tract infection, or gross hematuria. Seven to 14 days should elapse before BCG is administered following biopsy, TUR, or traumatic catheterization.

Active Tuberculosis

TICE BCG should not be administered to persons with active tuberculosis. Active tuberculosis should be ruled out in individuals who are PPD positive before starting treatment with TICE BCG.

WARNINGS

BCG LIVE (TICE® BCG) is not a vaccine for the prevention of cancer. BCG Vaccine, not BCG LIVE (TICE BCG), should be used for the prevention of tuberculosis. For vaccination use, refer to BCG Vaccine prescribing information.

Handling Precautions

TICE BCG is an infectious agent. Physicians using this product should be familiar with the literature on the prevention and treatment of BCG-related complications, and should be prepared in such emergencies to contact an infectious disease specialist with experience in treating the infectious complications of intravesical BCG. The treatment of the infectious complications of BCG requires long-term, multiple-drug antibiotic therapy. Special culture media are required for mycobacteria, and physicians administering intravesical BCG or those caring for these patients should have these media readily available.

BCG Infection

Instillation of TICE BCG with an actively bleeding mucosa may promote systemic BCG infection. Treatment should be postponed for at least 1 week following transurethral resection, biopsy, traumatic catheterization, or gross hematuria.

Systemic BCG Reaction

Deaths have been reported as a result of systemic BCG infection and sepsis.[2,3] Patients should be monitored for the presence of symptoms and signs of toxicity after each intravesical treatment. Febrile episodes with flu-like symptoms lasting more than 72 hours, fever ≥103°F, systemic manifestations increasing in intensity with repeated instillations, or persistent abnormalities of liver function tests suggest systemic BCG infection and may require antituberculous therapy. Local symptoms (prostatitis, epididymitis, orchitis) lasting more than 2 to 3 days may also suggest active infection (see **WARNINGS, Management of Serious BCG Complications** section).

Laboratory Tests

The use of TICE BCG may cause tuberculin sensitivity. Since this is a valuable aid in the diagnosis of tuberculosis, it is advisable to determine the tuberculin reactivity by PPD skin testing before treatment.

Antimicrobial Therapy

Intravesical instillations of BCG should be postponed during treatment with antibiotics, since antimicrobial therapy may interfere with the effectiveness of TICE BCG (see **PRECAUTIONS**). TICE BCG should not be used in individuals with concurrent infections.

Bladder Capacity

Small bladder capacity has been associated with increased risk of severe local reactions and should be considered in deciding to use TICE BCG therapy.

Management of Serious BCG Complications.

Acute, localized irritative toxicities of TICE BCG may be accompanied by systemic manifestations, consistent with a "flu-like" syndrome. Systemic adverse effects of 1 to 2 days' duration such as malaise, fever, and chills often reflect hypersensitivity reactions. However, **symptoms such as fever of ≥38.5°C (101.3°F), or acute localized inflammation such as epididymitis, prostatitis, or orchitis persisting longer than 2 to 3 days suggest active infection, and evaluation for serious infectious complication should be considered.**

In patients who develop persistent fever or experience an acute febrile illness consistent with BCG infection, 2 or more antimycobacterial agents should be administered while diagnostic evaluation, including cultures, is conducted. **BCG treatment should be discontinued.** Negative cultures do not necessarily rule out infection. Physicians using this product should be familiar with the literature on prevention, diagnosis, and treatment of BCG-related complications and, when appropriate, should consult an infectious disease specialist or other physician with experience in the diagnosis and treatment of mycobacterial infections.

TICE BCG is sensitive to the most commonly used antituberculous agents (isoniazid, rifampin, and ethambutol). **TICE BCG is not sensitive to pyrazinamide.**

PRECAUTIONS

General

TICE® BCG contains live mycobacteria and should be prepared and handled using aseptic technique (see **DOSAGE AND ADMINISTRATION, Preparation of Agent** section). BCG infections have been reported in health care workers preparing BCG for administration. Needle stick injuries should be avoided during the handling and mixing of TICE BCG. Nosocomial infections have been reported in patients receiving parenteral drugs which were prepared in areas in which BCG was prepared.[4]

BCG is capable of dissemination when administered by intravesical route, and serious reactions, including fatal infections, have been reported in patients receiving intravesical

BCG.[3] Care should be taken not to traumatize the urinary tract or to introduce contaminants into the urinary system. Seven to 14 days should elapse before TICE BCG is administered following TUR, biopsy, or traumatic catheterization.

TICE BCG should be administered with caution to persons in groups at high risk for HIV infection.

Laboratory Tests

The use of TICE BCG may cause tuberculin sensitivity. It is advisable to determine the tuberculin reactivity of patients receiving TICE BCG by PPD skin testing before treatment is initiated.

Information for Patients

TICE BCG is retained in the bladder for 2 hours and then voided. Patients should void while seated in order to avoid splashing of urine. For the 6 hours after treatment, urine voided should be disinfected for 15 minutes with an equal volume of household bleach before flushing. Patients should be instructed to increase fluid intake in order to "flush" the bladder in the hours following BCG treatment. Patients may experience burning with the first void after treatment.

Patients should be attentive to side effects, such as fever, chills, malaise, flu-like symptoms, or increased fatigue. If the patient experiences severe urinary side effects, such as burning or pain on urination, urgency, frequency of urination, blood in urine, or other symptoms such as joint pain, cough, or skin rash, the physician should be notified.

Drug Interaction

Drug combinations containing immunosuppressants and/or bone marrow depressants and/or radiation interfere with the development of the immune response and should not be used in combination with TICE BCG. Antimicrobial therapy for other infections may interfere with the effectiveness of TICE BCG. There are no data to suggest that the acute, local urinary tract toxicity common with BCG is due to mycobacterial infection, and **antituberculosis drugs (e.g., isoniazid) should not be used to prevent or treat the local, irritative toxicities of TICE BCG.**

Carcinogenesis, Mutagenesis, Impairment of Fertility

TICE BCG has not been evaluated for its carcinogenic, mutagenic potentials, or impairment of fertility.

Pregnancy

Animal reproduction studies have not been conducted with TICE BCG. It is also not known whether TICE BCG can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. TICE BCG should not be given to a pregnant woman except when clearly needed. Women should be advised not to become pregnant while on therapy.

Nursing Mothers

It is not known whether TICE BCG is excreted in human milk. Because many drugs are

excreted in human milk and because of the potential for serious adverse reactions from TICE BCG in nursing infants, it is advisable to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness of TICE BCG for the treatment of superficial bladder cancer in pediatric patients have not been established.

Geriatric Use

Of the total number of subjects in clinical studies of TICE BCG, the average age was 66 years old. No overall difference in safety or effectiveness was observed between older and younger subjects. Other reported clinical experience has not identified differences in response between elderly and younger patients, but greater sensitivity of some older individuals to BCG cannot be ruled out.

ADVERSE REACTIONS

Symptoms of bladder irritability, related to the inflammatory response induced, are reported in approximately 60% of patients receiving TICE® BCG. The symptoms typically begin 4 to 6 hours after instillation and last 24 to 72 hours. The irritative side effects are usually seen following the third instillation, and tend to increase in severity after each administration.

The irritative bladder adverse effects can usually be managed symptomatically with products such as pyridium, propantheline bromide, oxybutynin chloride, and acetaminophen. The mechanism of action of the irritative side effects has not been firmly established, but is most consistent with an immunological mechanism.[3] There is no evidence that dose reduction or antituberculous drug therapy can prevent or lessen the irritative toxicity of TICE BCG.

"Flu-like" symptoms (malaise, fever, and chills) which may accompany the localized, irritative toxicities often reflect hypersensitivity reactions which can be treated symptomatically. Antihistamines have also been used.[5]

Adverse reactions to TICE BCG tend to be progressive in frequency and severity with subsequent instillation. Delay or postponement of subsequent treatment may or may not reduce the severity of a reaction during subsequent instillation.

Although uncommon, serious infectious complications of intravesical BCG have been reported.[2,3,6] The most serious infectious complication of BCG is disseminated sepsis with associated mortality. In addition, *M. bovis* infections have been reported in lung, liver, bone, bone marrow, kidney, regional lymph nodes, and prostate in patients who have received intravesical BCG. Systemic infections may be manifested by pneumonitis, hepatitis, cytopenia, vasculitis, infective aneurysm and/or sepsis after a period of fever and malaise during which symptoms progressively increase. Some male genitourinary tract infections (orchitis/epididymitis) have been resistant to multiple-drug antituberculous therapy and required orchiectomy.

If a patient develops persistent fever or experiences an acute febrile illness consistent with BCG infection, BCG treatment should be discontinued and the patient immediately evaluated and treated for systemic infection (see

WARNINGS).

The local and systemic adverse reactions reported in a review of 674 patients with superficial bladder cancer, including 153 patients with carcinoma *in situ*, are summarized in **Table 5**.

Table 5: Summary of Adverse Effects Seen in 674 Patients With Superficial Bladder Cancer, Including 153 With Carcinoma in Situ

	Percent of patients			Percent of patients	
Adverse event	**N**	**Overall (Grade ≥3)**	**Adverse event**	**N**	**Overall (Grade ≥3)**
Dysuria	401	60% (11%)	Arthritis/myalgia	18	3% (<1%)
Urinary frequency	272	40% (7%)	Headache/dizziness	16	2%(0)
Flu-like syndrome	224	33% (9%)	Urinary incontinence	16	2% (0)
Hematuria	175	26% (7%)	Anorexia/weight loss	15	2% (<1%)
Fever	134	20% (8%)	Urinary debris	15	2% (<1%)
Malaise/fatigue	50	7% (0)	Allergy	14	2% (<1%)
Cystitis	40	6% (2%)	Cardiac (unclassified)	13	2% (1%)
Urgency	39	6% (1%)	Genital inflammation/		
Nocturia	30	5% (1%)	abscess	12	2% (<1%)
Cramps/pain	27	4% (1%)	Respiratory (unclassified)	11	2% (<1%)
Rigors	22	3% (1%)	Urinary tract infection	10	2% (1%)
Nausea/vomiting	20	3% (<1%)	Abdominal pain	10	2% (1%)

The following adverse events were reported in ≤1% of patients: anemia, BCG sepsis, coagulopathy, contracted bladder, diarrhea, epididymitis/prostatitis, hepatic granuloma, hepatitis, leukopenia, neurologic (unclassified), orchitis, pneumonitis, pyuria, rash, thrombocytopenia, urethritis, and urinary obstruction.

In SWOG study 8795, toxicity evaluations were available on a total of 222 TICE BCG-treated patients and 220 MMC-treated patients. Direct bladder toxicity (cramps, dysuria, frequency, urgency, hematuria, hemorrhagic cystitis, or incontinence) was seen more often with TICE BCG with 356 events, compared to 234 events for MMC. Grade ≤2 toxicity was seen significantly more frequently following TICE BCG treatment (P=0.003). No life-threatening toxicity was seen in either arm. Systemic toxicity with TICE BCG was markedly increased compared to that of MMC, with 181 events for TICE BCG compared to 80 for MMC. The frequency of toxicity was increased in all grades, particularly for grades 2 and 3. The most common complaints were malaise, fatigue and lethargy, fever, and abdominal pain. Thirty-two TICE BCG patients were reported to have been treated with isoniazid. Five TICE BCG patients had liver enzyme elevation, including 2 with grade 3 elevations. Eighteen of the 222 (8.1%) TICE BCG patients failed to complete the prescribed protocol compared to 6.2% in the MMC group. **Table 6** summarizes the most common adverse reactions reported in this trial.[7]

Table 6: Most Common Adverse Reactions in SWOG Study 8795*

	Study arm

	TICE BCG (N=222)		MMC (N=220)	
Adverse event	**All Grades**	**Grade ≥3**	**All Grades**	**Grade ≥3**
Dysuria	115 (52%)	6 (3%)	77 (35%)	5 (2%)
Urgency/frequency	112 (50%)	5 (2%)	63 (29%)	7 (3%)
Hematuria	85 (38%)	6 (3%)	56 (25%)	5 (2%)
Flu-like symptoms	54 (24%)	1 (<1%)	29 (13%)	0
Fever	37 (17%)	1 (<1%)	7 (3%)	0
Pain (not specified)	37 (17%)	4 (2%)	22 (10%)	1 (<1%)
Hemorrhagic cystitis	19 (9%)	3 (1%)	10 (5%)	0
Chills	19 (9%)	0	2 (1%)	0
Bladder cramps	18 (8%)	0	9 (4%)	0
Nausea	16 (7%)	0	12 (5%)	0
Incontinence	8 (4%)	0	3 (1%)	0
Myalgia/arthralgia	7 (3%)	0	0	0
Diaphoresis	7 (3%)	0	1 (<1%)	0
Rash	6 (3%)	1 (<1%)	16 (7%)	2 (1%)

* The adverse reaction profile of TICE BCG was similar in the Nijmegen study.[8]

Post-marketing Experience

The following adverse reactions have been identified during post-approval use of TICE BCG. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune System Disorders: hemophagocytic lymphohistiocytosis (HLH).

OVERDOSAGE

Overdosage occurs if more than 1 vial of TICE® BCG is administered per instillation. If overdosage occurs, the patient should be closely monitored for signs of active local or systemic BCG infection. For acute local or systemic reactions suggesting active infection, an infectious disease specialist experienced in BCG complications should be consulted.

DOSAGE AND ADMINISTRATION

The dose for the intravesical treatment of carcinoma *in situ* and for the prophylaxis of recurrent papillary tumors consists of 1 vial of TICE® BCG suspended in 50 mL preservative-free saline.

Do not inject subcutaneously or intravenously.

Preparation of Agent

The preparation of the TICE BCG suspension should be done using aseptic technique. To avoid cross-contamination, parenteral drugs should not be prepared in areas where BCG has been prepared. A separate area for the preparation of the TICE BCG suspension is recommended. All equipment, supplies, and receptacles in contact with

TICE BCG should be handled and disposed of as biohazardous. The pharmacist or individual responsible for mixing the agent should wear gloves and take precautions to avoid contact of BCG with broken skin. If preparation cannot be performed in a biocontainment hood, then a mask and gown should be worn to avoid inhalation of BCG organisms and inadvertent exposure to broken skin.

Draw 1 mL of sterile, preservative-free saline (0.9% Sodium Chloride Injection USP) at 4–25°C into a small syringe (e.g., 3 mL) and add to 1 vial of TICE BCG to resuspend. Ensure that the needle is inserted through the center of the rubber stopper of the vial. Gently swirl the vial until a homogenous suspension is obtained. Avoid forceful agitation which may cause clumping of the mycobacteria.

Dilute the cloudy TICE BCG suspension in sterile, preservative-free saline to a final volume of 50 mL. Mix the suspension gently prior to intravesical instillation.

The reconstituted TICE BCG should be kept refrigerated (2–8°C), protected from exposure to direct sunlight, and used within 2 hours. Discard unused portion.

Note: DO NOT filter the contents of the TICE BCG vial. Precautions should be taken to avoid exposing the TICE BCG to direct sunlight. Bacteriostatic solutions must be avoided. In addition, use only sterile, preservative-free saline, 0.9% Sodium Chloride Injection USP as diluent.

Treatment and Schedule

Allow 7 to 14 days to elapse after bladder biopsy before TICE BCG is administered. Patients should not drink fluids for 4 hours before treatment and should empty their bladder prior to TICE BCG administration. The reconstituted TICE BCG is instilled into the bladder by gravity flow via the catheter. After instillation of the TICE BCG suspension is complete, remove the catheter. The TICE BCG is retained in the bladder for 2 hours and then voided. Patients unable to retain the suspension for 2 hours should be allowed to void sooner, if necessary.

While the BCG is retained in the bladder, the patient ideally should be repositioned from left side to right side and also should lie upon the back and the abdomen, changing these positions every 15 minutes to maximize bladder surface exposure to the agent.

A standard treatment schedule consists of 1 intravesical instillation per week for 6 weeks. This schedule may be repeated once if tumor remission has not been achieved and if the clinical circumstances warrant. Thereafter, intravesical TICE BCG administration should continue at approximately monthly intervals for at least 6 to 12 months. There are no data to support the interchangeability of BCG LIVE products.

HOW SUPPLIED

TICE® BCG is supplied in a box of 1 single-dose vial of TICE BCG. Each vial contains 1 to 8×10^8 CFU, which is equivalent to approximately 50 mg (wet weight), as lyophilized (freeze-dried) powder, NDC 0052-0602-02.

STORAGE

The intact vials of TICE® BCG should be stored refrigerated, at 2–8°C (36–46°F).

This agent contains live bacteria and should be protected from **direct** sunlight. The product should not be used after the expiration date printed on the label.

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For patent information: www.msd.com/research/patent

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PRINCIPAL DISPLAY PANEL - 50 mL Vial Carton

NDC 0052-0602-02

BCG
LIVE

(for Intravesical Use)

TICE®
BCG

Rx only

Single-Dose Vial

TICE BCG

bacillus calmette-guerin powder, for suspension

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0052-0602
Route of Administration	INTRAVESICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
BACILLUS CALMETTE-GUERIN SUBSTRAIN TICE LIVE ANTIGEN (UNII: 2XQ558L16Z) (BACILLUS CALMETTE-GUERIN SUBSTRAIN TICE LIVE ANTIGEN - UNII:2XQ558L16Z)	BACILLUS CALMETTE-GUERIN SUBSTRAIN TICE LIVE ANTIGEN	50 mg in 50 mL

Inactive Ingredients

Ingredient Name	Strength
GLYCERIN (UNII: PDC6A3C0OX)	
ASPARAGINE (UNII: 5Z33R5TKO7)	
CITRIC ACID MONOHYDRATE (UNII: 2968PHW8QP)	
POTASSIUM PHOSPHATE, UNSPECIFIED FORM (UNII: B7862WZ632)	
MAGNESIUM SULFATE, UNSPECIFIED FORM (UNII: DE08037SAB)	
LACTOSE, UNSPECIFIED FORM (UNII: J2B2A4N98G)	
FERRIC AMMONIUM CITRATE (UNII: UVP74NG1C5)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0052-0602-02	1 in 1 CARTON	08/24/1990	
1	NDC:0052-0602-01	50 mL in 1 VIAL; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA102821	08/24/1990	

Labeler - Merck Sharp & Dohme LLC (118446553)

Revised: 2/2026 Merck Sharp & Dohme LLC