Intravesical Bacillus Calmette-Guerin: Drug information

(For additional information see "Intravesical Bacillus Calmette-Guerin: Patient drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

ALERT: US Boxed Warning

Biohazard agent:

BCG (intravesical) contains live, attenuated mycobacteria. Because of the potential risk for Bacillus Calmette Guerin (BCG) transmission, prepare, handle, and dispose of as a biohazard material.

Disseminated infections:

BCG dissemination may occur when administered by the intravesical route. Serious infections, including fatal infections, have been reported. BCG may persist in the urinary tract for several months after BCG instillations and delayed manifestations of disseminated BCG infection may develop months or years after BCG therapy.

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 (intravesical) for administration. Nosocomial infections have been reported in patients receiving parenteral drugs that were prepared in areas where BCG (intravesical) was reconstituted.

Brand Names: US

TheraCys; Tice BCG

Brand Names: Canada

ImmuCyst; Oncotice

Pharmacologic Category

Antineoplastic Agent, Biological Response Modulator

Dosing: Adult

Bladder cancer: Intravesicular:

TheraCys: Induction: One dose (81 mg or one vial) instilled into bladder (retain for up to 2 hours) once weekly for 6 weeks beginning at least 14 days after biopsy or transurethral resection, followed by maintenance therapy of 81 mg (one vial) at 3, 6, 12, 18, and 24 months after initial dose.

TICE BCG: Induction: One dose (~50 mg or one vial) instilled into the bladder (retain for 2 hours) once weekly for 6 weeks beginning 7 to 14 days after biopsy (may repeat cycle 1 time if tumor remission not achieved), followed by maintenance therapy of ~50 mg (one vial) approximately once a month for at least 6 to 12 months.

Dosing: Geriatric Refer to adult dosing.

Dosing: Renal Impairment There are no dosage adjustments provided in the manufacturer's labeling.

Dosing: Hepatic Impairment There are no dosage adjustments provided in the manufacturer's labeling.

Dosing: Adjustment for Toxicity

Bacterial urinary tract infection: Withhold treatment until complete resolution.

Persistent fever or acute febrile illness consistent with BCG infection: Discontinue treatment.

Dosage Forms Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Suspension Reconstituted, Intravesical:

Tice BCG: 50 mg (1 ea)

Suspension Reconstituted, Intravesical [preservative free]:

TheraCys: 81 mg (1 ea) [contains monosodium glutamate (sodium glutamate)]

Generic Equivalent Available (US) No

Administration For intravesicular (bladder instillation) administration only; **do not administer IV, SubQ, IM, or intradermally**.

Intravesicular: Patients should not drink fluids for 4 hours prior to instillation. Empty or drain bladder. Instill BCG (intravesical) by gravity; retain for as long as possible, up to 2 hours. Patient should lie prone for at least 15 minutes, then rotate positions (lie on right side, left side, abdomen, and back) every 15 minutes to maximize bladder surface exposure (TICE BCG); for TheraCys, patient may be in an upright position after the first 15 minutes. Following bladder instillation, patients should be instructed to void in a seated position in order to avoid the splashing of urine; burning may occur with the first void following therapy. Prior to flushing, disinfect the urine for 15 minutes with an equal amount of household bleach (this should be done for the first 6 hours after therapy). After administration, patients should drink plenty of water in order to flush the bladder.

Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage.

NIOSH recommends double gloving, a protective gown, and preparation in a controlled device or use of ventilated engineering controls (a class II biological safety cabinet or a compounding aseptic containment isolator); if not prepared in a controlled device, respiratory and eye/face protection as well as ventilated

engineering controls are recommended. NIOSH recommends double gloving, a protective gown, and eye/face and respiratory protection for intravesical administration (NIOSH 2016).

Use

Bladder cancer: Treatment and prophylaxis of carcinoma in situ of the urinary bladder; prophylaxis of primary or recurrent superficial or minimally invasive (stage Ta and/or T1) papillary tumors following transurethral resection

Limitations of use: BCG (intravesical) is not recommended for stage Ta low-grade papillary tumors unless judged to be at high risk for recurrence. BCG (intravesical) is not recommended for immunization against tuberculosis.

Medication Safety Issues

Sound-alike/look-alike issues:

BCG (intravesical) may be confused with BCG vaccine (immunization)

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Adverse Reactions

>10%:

Central nervous system: Malaise (≤40%), chills (9% to 34%), pain (≤17%)

Gastrointestinal: Nausea (≤16%), vomiting (≤16%), anorexia (≤11%)

Genitourinary: Dysuria (52% to 60%), irritable bladder (50% to 60%), urinary frequency (40% to ≤50%), urinary urgency (6% to ≤50%), hematuria (26% to 39%), cystitis (6% to 30%), urinary tract infection (2% to 18%)

Hematologic & oncologic: Anemia (≤21%)

Respiratory: Flu-like symptoms (24% to 33%)

Miscellaneous: Fever (17% to 38%)

1% to 10%:

Central nervous system: Fatigue (≤7%), dizziness (≤2%), headache (≤2%)

Dermatologic: Diaphoresis (3%), skin rash (≤3%)

Endocrine & metabolic: Weight loss (≤2%)

Gastrointestinal: Diarrhea (≤6%), abdominal pain (2% to 3%)

Genitourinary: Genital pain (10%), nephrotoxicity (10%), hemorrhagic cystitis (9%), bladder spasm (≤8%; including contracted bladder), bladder pain (≤6%), urinary incontinence (2% to 6%), nocturia (5%), bladder contraction (≤5%), urine sedimentation abnormality (debris and tissue; ≤2%), epididymitis (≤1%), orchitis (≤1%), prostatitis (≤1%), pyuria (≤1%), urethritis (≤1%), urinary tract obstruction (≤1%)

Hematologic & oncologic: Leukopenia (≤5%), blood coagulation disorder (≤1%); thrombocytopenia (≤1%)

Hepatic: Granulomatous hepatitis (≤1%), hepatitis (≤1%)

Hypersensitivity: Hypersensitivity (2%)

Infection: Sepsis (3%; BCG sepsis: ≤1%), abscess (genital; ≤2%)

Neuromuscular & skeletal: Arthritis (≤7%), arthralgia (≤7%), myalgia (≤7%), muscle cramps (≤4%), rigors (3%)

Respiratory: Pulmonary infection (3%), pneumonitis (≤1%)

Miscellaneous: Inflammation (genital; ≤2%)

<1%, postmarketing, and/or case reports: Arthritis (reactive), chorioretinitis (granulomatous), conjunctivitis, constipation, erythema nodosum, flank pain, increased blood urea nitrogen, increased serum creatinine, infection (including systemic mycobacterium bovis infection of bone, bone marrow, kidney, lung, liver, lymph nodes, prostate), interstitial pulmonary disease, iritis, keratitis, localized infection (renal abscess), nephritis (includes glomerulonephritis, interstitial nephritis, renal tubulo-interstitial nephritis), pneumonia, pyelonephritis, renal failure, urinary retention (includes bladder tamponade and increased post-void residual urine volume), uveitis

Contraindications Known hypersensitivity to BCG (intravesical) or any component of the formulations, hypersensitivity after a previous administration of BCG (intravesical) or after a previous administration of a medicinal product containing the same substances; immunosuppressed patients or persons with congenital or acquired immune deficiencies (eg, HIV infection, leukemia, lymphoma, cancer therapy, immunosuppressive therapy such as corticosteroids); active tuberculosis; concurrent febrile illness, urinary tract infection, or gross hematuria; current symptoms or previous history of a systemic BCG reaction; recent (TheraCys: <14 days; TICE BCG: <7 to 14 days) biopsy, transurethral resection (TUR), or traumatic catheterization

Warnings/Precautions

Concerns related to adverse effects:

• BCG reaction: A systemic granulomatous illness occurring following exposure to BCG is referred to as a systemic BCG reaction when any of the following are present without another detectable etiology: Fever ≥39.5°C for ≥12 hours or ≥38.5°C for ≥48 hours; pneumonitis; hepatitis; organ dysfunction outside of the GU tract with granulomatous inflammation; clinical signs of sepsis. It may be difficult to determine if reaction is due to infection process or inflammatory hypersensitivity. A systemic BCG reaction is more likely to occur with intravesical administration <14 days after a biopsy, transurethral resection (TUR), or traumatic catheterization. Fatalities have been reported with systemic BCG reactions.

• Bladder irritation: BCG (intravesical) may cause symptoms of bladder irritability which usually begin 4 to 6 hours after instillation and may last 24 to 72 hours; symptoms may increase in severity following each instillation.

• Disseminated infections: **[US Boxed Warning]: May cause disseminated (including fatal) infections following intravesical administration.** Instillation to actively bleeding mucosa may promote systemic BCG infection or sepsis. To prevent serious infections, avoid trauma and/or introduction of contaminants into the urinary tract; postpone treatment for at least 1 to 2 weeks (depending on product) following TUR, biopsy, traumatic catheterization (may resume original schedule after 14 days), or gross hematuria. Do not use in patients with concurrent infections. Use caution in patients with aneurysms and prosthetic devices; ectopic BCG infection may occur at these sites. If signs and symptoms of a systemic BCG infection occur, permanently discontinue BCG treatment and begin therapy with 2 or more antimycobacterial agents (do not use single-agent therapy) while conducting a diagnostic evaluation. Infection from BCG (intravesical) is not sensitive to pyrazinamide. Do not use prophylactic antimycobacterial therapy to prevent local adverse events during treatment (there is no data to support use and may alter efficacy). Determine PPD status prior to use (rule out active tuberculosis prior to treatment initiation). Prior to intravesical instillation, patients with a positive PPD test should be further assessed for signs and/or symptoms of active or latent tuberculosis. BCG may persist in the urinary tract for several months after treatment; delayed manifestations of disseminated BCG infection may develop months to years after BCG therapy. Patients who receive immunosuppressive therapy after BCG therapy may be at higher risk for disseminated infection. Monitor for signs/symptoms of infection/toxicity after each treatment. Discontinue for persistent fever or acute febrile illness consistent with BCG infection. Some male genitourinary tract infections (orchitis or epididymitis) have been refractory to multiple antituberculosis drug therapies and have required orchiectomy.

Disease-related concerns:

• Small bladder capacity: Intravesical instillation may be associated with increased risk of severe local reactions in the presence of small bladder capacity; use with caution.

• Urinary tract infection: If a bacterial urinary tract infection occurs during therapy, withhold instillation until complete resolution of infection.

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Dosage form specific issues:

• Latex: Packaging may contain natural latex rubber.

Special handling:

• Biohazard agent: **[US Boxed Warning]: Contains live, attenuated mycobacteria. Use appropriate precautions for handling and disposal. BCG is a biohazard; proper preparation technique, handling, and disposal of all equipment in contact with BCG as a biohazard material is recommended.** BCG infections have been reported in health care workers due to accidental exposure (needle stick, skin laceration); nosocomial infections have been reported in patients (including immunosuppressed patients) receiving parenteral medications prepared in areas

where BCG was prepared. To avoid cross contamination, do not prepare parenteral medications in an area where BCG has been prepared.

Other warnings/precautions:

• Appropriate use: BCG (intravesical) is not a vaccine for the prevention of cancer. Information is not available for interchanging products used for intravesical administration.

Metabolism/Transport Effects

None known.

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Antibiotics: May diminish the therapeutic effect of BCG (Intravesical). **Exceptions:** Acetic Acid (Otic); Acetic Acid (Topical); Aluminum Acetate; Azithromycin (Ophthalmic); Aztreonam (Oral Inhalation); Bacitracin (Ophthalmic); Bacitracin (Topical); Ciprofloxacin (Ophthalmic); Clindamycin (Topical); Dapsone (Topical); Erythromycin (Ophthalmic); Erythromycin (Topical); Fidaxomicin; Framycetin; Fusidic Acid (Ophthalmic); Fusidic Acid (Topical); Gatifloxacin; Gentamicin (Ophthalmic); Gentamicin (Topical); MetroNIDAZOLE (Topical); Mupirocin; Nitrofurazone; Sulfacetamide (Ophthalmic); Tobramycin (Ophthalmic). *Risk X: Avoid combination*

Hexaminolevulinate: BCG (Intravesical) may diminish the diagnostic effect of Hexaminolevulinate. *Risk X: Avoid combination*

Immunosuppressants: May diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

Myelosuppressive Agents: May diminish the therapeutic effect of BCG (Intravesical). *Risk X: Avoid combination*

Pregnancy Risk Factor

C (show table)

Pregnancy Implications

Animal reproduction studies have not been conducted. BCG (intravesical) is not recommended for use in pregnant women. Women of childbearing potential should be advised to avoid pregnancy while on BCG (intravesical) therapy.

Breast-Feeding Considerations

It is not known if BCG (intravesical) is excreted in breast milk. Due to the potential for serious adverse reactions in the nursing infant, a decision should be made to discontinue breast-feeding or avoid use of BCG (intravesical), taking into account the importance of BCG (intravesical) to the mother.

Monitoring Parameters

PPD test prior to treatment

Intravesical treatment: Monitor for signs/symptoms of toxicity/infection following every treatment. Signs that antituberculous therapy may be needed: Flu-like symptoms ≥72 hours, fever ≥101.3°F, systemic symptoms which worsen with each treatment, persistently abnormal liver function tests, prostatitis, epididymitis or orchitis of >2 to 3 day duration

Mechanism of Action

BCG (intravesical) is an attenuated strain of bacillus Calmette-Guérin (*Mycobacterium bovis*) used as a biological response modifier. BCG, when used intravesicularly for treatment of bladder carcinoma *in situ*, is thought to cause a local, chronic inflammatory response involving macrophage and leukocyte infiltration of the bladder. BCG (intravesical) is active immunotherapy which stimulates the host's immune mechanism to reject the tumor.

Pricing: US

Suspension (reconstituted) (TheraCys Intravesical)

81 mg/vial (1): $204.79

Suspension (reconstituted) (Tice BCG Intravesical)

50 mg (1): $177.66

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names

BCG-Medac (TH); Immucyst (AR, AT, AU, BE, BG, CH, CN, CO, CZ, DE, EC, EE, ES, FR, GB, GR, HK, HN, HR, HU, IL, IT, KR, LB, MY, NZ, PT, PY, RO, SG, SI, SK, TH, TR, TW, VN)

REFERENCES

1. *TheraCys (BCG) [prescribing information]. Swiftwater, PA: Sanofi Pasteur; November 2015.*
2. *TICE BCG [prescribing information]. Whitehouse Station, NJ: Merck Sharpe & Dohme; March 2016.*
3. *US Department of Health and Human Services; Centers for Disease Control and Prevention; National Institute for Occupational Safety and Health. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2016. http://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf. Updated September 2016. Accessed October 5, 2016.*

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