New Century Health

POLICY#UM_1046
PROPRIETARY&CONFIDENTIAL

POLICY NUMBER UM_1046	**SUBJECT** Bacillus Calmette-Guerin (BCG)		**DEPT/PROGRAM** UM Dept.	**PAGE 1 OF 3**
DATE REVIEWED 10/05/11, 04/10/13, 07/10/14, 12/17/15, 08/22/16, 06/06/17, 06/08/18, 05/03/19	**APPROVAL DATE** May 8, 2019	**EFFECTIVE DATE** May 8, 2019	**REVISION DATES** (latest version listed last) 02/20/11, 10/05/11, 04/10/13, 12/17/15, 08/25/16, 05/08/19	
PRIMARY BUSINESS OWNER: UM **APPROVED BY:** Dr. Andrew Hertler		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
URAC STANDARDS HUM 1		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Oncology	

I. PURPOSE

To define and describe the accepted indications for Bacillus Calmette-Guerin (BCG) usage in the treatment of cancer.

II. DEFINITIONS

Bacillus Calmette-Guerin (BCG): is an immunostimulant. BCG treatment is used to mount a local inflammation and immune reaction against superficial cancers, but the exact mechanism of action is unknown. The Calmette-Guerin strain of Mycobacterium bovis present in BCG Live is immunologically similar to M. tuberculosis. Intravesical BCG produces a non-specific, localized immune reaction consisting of granulomatous and inflammation reactions with histocyte and leukocyte infiltration. Following intravesical administration, the live BCG mycobacteria attach to the urothelial lining. The bacterial cell surface glycoproteins act as antigens that stimulate the immune response including macrophages, T-lymphocytes, B-lymphocytes, natural killer cells, and killer cells. This leads the production of interleukin (IL)-1, IL-2, IL-6, interferon gamma, and tumor necrosis factor-alpha (TNF-alpha). The immunotherapeutic effects of BCG in bladder cancer are due to cytokines, which cause cytotoxic effects. Tumor cell motility is also thought to be inhibited. Biopsies following BCG administration show increased expression of human leukocyte antigen (HLA)-Dr on tumor cells and infiltration of tumor and stroma with lymphocytes, mostly T-helper cells, and macrophages. Systemically, an increased immune response to the BCG antigen and production of BCG antibody may be seen

Bacillus Calmette-Guerin (BCG) is indicated for intravesical use in the treatment and prophylaxis of carcinoma in situ (CIS) of the urinary bladder and for the prophylaxis of primary or recurrent stage Ta and/or T1 papillary tumors following transurethral resection (TUR). BCG is not recommended for stage TaG1 papillary tumors, unless they are judged to be at high risk of tumor recurrence.

BCG is available as TICE. Each vial contains 1 to 8 × 10^8 CFU, which is equivalent to approximately 50 mg (wet weight), as lyophilized (freeze-dried) powder.

III. POLICY

New Century is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century may be deemed as not approvable and therefore not reimbursable.

Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Bacillus Calmette-Guerin (BCG) may be considered medically necessary when any of the following selection criteria is met:

1. **Bladder Cancer**
    a. The member has carcinoma in situ (CIS), clinical stage Ta, Tis, or T1 tumor of the urinary bladder and Bacillus Calmette-Guerin (BCG) is being used as **ONE** of the following:
        i. Adjuvant treatment as intravesical immunotherapy for ONE of the following nonmuscle-invasive papillary or solid tumors:
            1. Clinical stage Ta
            2. Re-resected clinical stage T1 tumors
            3. Any Tis abnormal mucosa
        ii. Recurrent or persistent disease (cytology and bladder-biopsy positive, imaging and cystoscopy negative) after initial intravesical treatment for Tis, clinical stage Ta, or T1 tumors.
        iii. Maintenance therapy following initial adjuvant treatment for Tis, clinical stage Ta, or T1 tumors in member with
            1. Recurrent or persistent disease (cytology positive, imaging and cystoscopy negative) after initial intravesical treatment OR
            2. Recurrent disease with no residual disease following intravesical treatment with BCG or mitomycin (no more than 2 consecutive treatments).
        iv. Treatment for local recurrence or persistent disease as clinical stage Ta or T1 or Tis following bladder-sparing treatment for muscle-invasive disease and selected metastatic disease treated with curative intent
        v. Treatment for recurrent Tis or clinical stage Ta disease or for high-grade clinical T1 disease following intravesical treatment with mitomycin (no more than 2 consecutive cycles).

Exclusion Criteria: Bacillus Calmette-Guerin (BCG) is not considered medically necessary when any of the following selection criteria is met:

1. BCG is being used as an immunizing agent for the prevention of tuberculosis.
2. BCG is being used in member with active tuberculosis (active tuberculosis should be ruled out in individuals who are PPD positive before starting treatment with BCG).
3. BCG is being used for papillary tumors of stages higher than T1.
4. BCG is being used in immunosuppressed member or member 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).
5. Bacillus Calmette-Guerin (BCG) is being used concurrently with Mitomycin C or Valrubicin intravesically.
6. Dosing exceeds single dose limit of Tice 50 mg or TheraCys 81 mg.
7. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Bacillus Calmette-Guerin (BCG) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration**
    a. TICE BCG: 1 vial (50 mg) intravesically 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, maintenance intravesical BCG administration should continue at approximately monthly intervals for at least 6 to 12 months.
2. **Dosage Adjustments:**
    a. 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.
    b. Intravesical instillations of BCG should be postponed during treatment with antibiotics, since antimicrobial therapy may interfere with the effectiveness of BCG. BCG should not be used in individuals with concurrent infections.
3. **Monitoring**
    a. BCG contains live, attenuated mycobacteria. Because of the potential risk for transmission, it should be prepared, handled, and disposed of as a biohazard material.
    b. 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 member 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 member receiving intravesical BCG.
    c. 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.

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Clinical Pharmacology Elsevier Gold Standard. 2018.
2. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019.
3. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2019.
4. TheraCys® BCG prescribing information. Sanofi Pasteur Inc. Swiftwater, PA, 2019.
5. TICE® BCG prescribing information. Organon Teknika Corporation LLC. Durham, NC. 2019.