

הנדון: OncoTICE
אונקוטייס**Dosage Form:** Powder for Solution for Instillation
Composition: BCG Strain 200 – 800 MIU

חברת מרק שארפ ודוהם (ישראל-1996) בע"מ (MSD ישראל), מבקשת ליידע על עדכון העלון לרופא ולצרכן של OncoTICE להכללת העדכונים עפ"י המפורט מטה.

להלן לשון ההתוויה המאושרת לתכשיר:

OncoTICE is used as a treatment of flat urothelial cell carcinoma in situ (CIS) of the bladder and as an adjuvant therapy after transurethral resection (TUR) of a primary or relapsing superficial papillary urothelial cell carcinoma of the bladder stage Ta (grade 2 or 3) or T1 (grade 1 2 or 3).
OncoTICE is only recommended for stage Ta grade 1 papillary tumors when there is judged to be a high risk of tumor recurrence.

טקסט מהותי שהתווסף מודגש בקו תחתון.

עדכונים מהותיים שבוצעו בעלון לרופא:

הוספת קופסת אזהרה בראש העלון:

WARNING

OncoTICE contains live, attenuated mycobacteria. Because of the potential risk for transmission, prepare, handle, and dispose of OncoTICE as a biohazard material (see sections 4.2 and 4.4).

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 sections 4.4 and 4.8).

4. CLINICAL PARTICULARS

[...]

4.4 Special warnings and special precautions for use

[...]

Handling Precautions

OncoTICE 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 OncoTICE 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. 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 above 39°C, 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) last for 48 to 72 hours may also suggest active infection (see **WARNINGS, Management of Serious BCG Complications** section).

Management of Serious BCG Complications.

Acute, localized irritative toxicities of OncoTICE 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 above 39°C, or acute localized inflammation such as epididymitis, prostatitis, or orchitis persisting longer than 48 to 72 hours 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.

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

[...]

4.8 Undesirable effects

[...]

Although uncommon, serious infectious complications of intravesical BCG have been reported. 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 section 4.4).

עדכונים מהותיים שבוצעו בעלון לצרכן:

הוספת קופסת אזהרה בראש העלון:

אזהרה

אונקוטייס מכילה חיידק מיקובקטריה חי מוחלש. בשל הסיכון האפשרי להעברה, יש להכין, לטפל ולהיפטר מאונקוטייס כנהוג עם חומר ביולוגי מסוכן (Biohazard material).
זיהומי BCG דווחו בעובדי צוות רפואי, בעיקר בעקבות חשיפות כתוצאה מדקירות מחט לא מכוונות או חתכים בעור במהלך ההכנה למתן של BCG.
זיהומים נזדקומיאליים (זיהומים שמקורם בבית חולים) דווחו במטופלים שקיבלו תרופות בדרך מתן פרנטרלית (שאינה דרך הפה), אשר הוכנו באזורים בהם הוכנה תמיסת BCG. BCG יכול להתפזר בגוף כאשר ניתן ישירות לשלפוחית (מתן אינטרה-וזיקאלי), וזיהומים חמורים כולל זיהומים מסכני חיים, דווחו במטופלים אשר קיבלו BCG במתן ישירות לשלפוחית.

הוספת הוראות לצוות רפואי בסוף העלון:

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 $2-8 \times 10^8$ CFU of Tice BCG.

למידע מלא ולהוראות מתן מפורטות, יש לעיין בעלון לרופא ולצרכן המאושרים על ידי משרד הבריאות.

העלונים לרופא ולצרכן נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום, חברת MSD, בטלפון 09-9533333.
OncoTICE מופצת ע"י חברת נובולוג בע"מ.

בברכה,
מורן שגיא
רוקחת ממונה
MSD ישראל

References:

OncoTICE-SPC-05_2024_clean

OncoTICE-PIL-HEB-05_2024_clean