ינואר 2021

רופא/ה יקר/ה,
רוקח/ת יקר/ה,

הנדון: <u>אינבנז - INVANZ®</u>

Dosage form: Lyophillized Powder for Injection
Composition: Ertapenem (as sodium) 1 gr/vial

חברת מרק שארפ ודוהם (ישראל-1996) בע"מ, (MSD ישראל), מבקשת ליידע על עדכון העלון לרופא של התכשיר INVANZ.

להלן לשון ההתוויות המאושרות לתכשיר:
Invanz is indicated for the treatment of adult patients and pediatric patients (3 months of age and older) with the following moderate to severe infections caused by susceptible isolates of the designated microorganisms.
- Complicated intra-abdominal infections.
- Complicated skin and skin structure infections including diabetic foot infections without osteomyelitis.
- Community acquired pneumonia.
- Complicated urinary tract infections including pyelonephritis.
- Acute pelvic infections including postpartum endomyometritis septic abortion and post surgical gynecologic infections.

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

<u>עדכונים מהותיים שבוצעו בעלון לרופא:</u>
טקסט שהוסף מודגש בקו תחתון, טקסט שנמחק מסומן בקו חוצה.

12.4 Microbiology
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בסעיף "Susceptibility Testing Methods" הטקסט הקיים הוחלף עם הפניה לאתר ה -FDA כמפורט בזאת:

~~*Susceptibility Test Methods:*~~ <u>Susceptibility Testing</u>
<u>For specific information regarding susceptibility testing methods, interpretive criteria, and associated test methods and quality control standards recognized by FDA for ertapenem, please see: https://www.fda.gov/STIC.</u>
~~When available, the clinical microbiology laboratory should provide the results of *in vitro* susceptibility tests for antimicrobial drug products used in resident hospitals to the physician as periodic reports which describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting the most effective antimicrobial.~~
~~Dilution Techniques:~~
~~Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized procedure. Standardized procedures are based on a broth dilution method {1} or equivalent with standardized inoculum concentrations and standardized concentrations of ertapenem powder. The MIC values should be interpreted according to criteria provided in Table 11 and {4}.~~
~~Diffusion Techniques:~~
~~Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure {2} requires the use of standardized inoculum concentrations. This procedure uses paper disks impregnated with 10-µg ertapenem to test the susceptibility of microorganisms to ertapenem. The disk diffusion interpretive criteria should be interpreted according to criteria provided in Table 11 and {4}.~~
~~Anaerobic Techniques:~~
~~For anaerobic bacteria, the susceptibility to ertapenem as MICs can be determined by standardized test methods {3}. The MIC values obtained should be interpreted according to criteria provided in Table 11 and {4}.~~

~~Table 11~~
~~Susceptibility Interpretive Criteria for Ertapenem~~

~~Pathogen~~	~~Minimum Inhibitory Concentrations* MIC (µg/mL)~~	~~Disk Diffusion Zone Diameter (mm)~~

	S	I	R	S	I	R
Enterobacteriaceae	≤0.5	1	≥2	≥22	19-21	≤18
Staphylococcus aureus†	≤2.0	4.0	≥8.0	≥19	16-18	≤15
Haemophilus spp.*	≤0.5	-	-	≥19	-	-
Streptococcus pneumoniae‡	≤1.0	2	≥4	-	-	-
Streptococcus spp. Beta Hemolytic Group*†§	≤1.0	-	-	-	-	-
Streptococcus spp. Viridans Group*	≤1.0	-	-	-	-	-
Anaerobes	≤4.0	8.0	≥16.0	-	-	-

* For some organism/antimicrobial combinations, the absence or rare occurrence of resistant strains precludes defining any results categories other than "susceptible". For strains yielding results suggestive of a "non-susceptible" category, organism identification and antimicrobial susceptibility test results should be confirmed.

† For oxacillin-susceptible *S. aureus* results for carbapenems, including ertapenem, if tested, should be reported according to the results generated using routine interpretive criteria. For oxacillin-resistant *S. aureus* and coagulase negative staphylococci, other beta lactam agents, including carbapenems, may appear active *in vitro* but are not effective clinically. Results for beta lactam agents other than cephalosporins with anti-MRSA activity should be reported as resistant or should not be reported.

‡ *S. pneumoniae* penicillin MICs ≤2 mcg/mL indicate susceptibility to ertapenem.

§ A beta hemolytic *Streptococcus* spp. (Groups A, B, C, G) isolate susceptible to penicillin (MIC ≤0.12 μg/mL) can be considered susceptible to ertapenem and need not be tested against ertapenem.

A report of "Susceptible" indicates that the pathogen is likely to be inhibited if the antimicrobial compound at the infection site reaches the concentrations usually achievable. A report of "Intermediate" indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone which prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of "Resistant" indicates that the pathogen is not likely to be inhibited if the antimicrobial compound at the infection site reaches the concentrations usually achievable; other therapy should be selected.

Quality Control

Standardized susceptibility test procedures require the use of laboratory control microorganisms to ensure the accuracy and precision of supplies and reagents used in the assay, and the techniques of the individuals performing the test. Quality control microorganisms are specific strains of organisms with intrinsic biological properties. QC strains are very stable strains which will give a standard and repeatable susceptibility pattern. The specific strains used for microbiological quality control are not clinically significant. Standard ertapenem powder should provide the following range of values noted in Table 12 and {4}.

Table 12
Acceptable Quality Control Ranges for Ertapenem

Microorganism	Minimum Inhibitory Concentrations MIC Range (μg/mL)	Disk Diffusion Zone Diameter (mm)
Escherichia coli ATCC 25922	0.004-0.016	29-36
Haemophilus influenzae ATCC 49766	0.015-0.06	27-33
Staphylococcus aureus ATCC 29213	0.06-0.25	-
Staphylococcus aureus ATCC 25923	-	24-31
Streptococcus pneumoniae ATCC 49619	0.03-0.25	28-35
Bacteroides fragilis ATCC 25285	0.06-0.5* 0.06-0.25†	-
Bacteroides thetaiotaomicron ATCC 29741	0.5-2.0* 0.25-1.0†	-
Eubacterium lentum ATCC 43055	0.5-4.0* 0.5-2.0†	-

* Quality control ranges for broth microdilution testing

† Quality control ranges for agar dilution testing

בעלון לרופא היו עדכונים נוספים שאינם מהותיים ואינם נכללים בהודעה זו. העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על ידי פניה לבעל הרישום, חברת MSD ישראל, בטלפון 09-9533333.
INVNAZ מופץ ע"י חברת נובולוג בע"מ.

בברכה,

אורית בילין
רוקחת ממונה
MSD ישראל

Refrences:
INVANZ SPC 01/2021