פייזר פי אף אי פרמצבטיקה ישראל בע"מ
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יולי 2022

רופא/ה, רוקח/ת נכבד/ה,

ברצוננו להודיעך על עדכון בעלון לרופא של **Zavicefta ; זביספטה**:

הודעה זו כוללת את המידע הנוגע לשינוי ביציבות לאחר פתיחה ודילול והוראות ההכנה של התכשיר (מסומנים בקו תחתון בגוף ההודעה), וכן עדכונים המהווים החמרה במידע הבטיחותי (מסומנים עם רקע צהוב בגוף ההודעה) , למידע מלא יש לעיין בעלון המאושר.

המרכיבים הפעילים:

ceftazidime pentahydrate equivalent to 2 g ceftazidime
avibactam sodium equivalent to 0.5 g avibactam

Indicated for:
Zavicefta® is indicated for the treatment of the following infections in adults:

- *Complicated intra-abdominal infection (cIAI), used in combination with Metronidazole*
- *Complicated urinary tract infection (cUTI), including pyelonephritis*
- *Hospital-acquired pneumonia (HAP), including ventilator associated pneumonia (VAP)*

Zavicefta® is also indicated for the treatment of infections due to aerobic Gram-negative organisms in adult patients with limited treatment options (see sections 4.2, 4.4 and 5.1).

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

להלן העדכונים העיקריים בעלון לרופא:

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Excipient with known effect:
Zavicefta contains approximately 146 mg sodium per vial

4.4 Special warnings and precautions for use

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Controlled sodium diet

This medicinal product contains approximately 146 mg sodium per vial, equivalent to 7.3% of the WHO recommended maximum daily intake (RDI) of 2 g sodium for an adult. The maximum daily dose of this product is equivalent to 22% of the WHO recommended maximum daily intake for sodium. Zavicefta is considered high in sodium.
This should be considered when administering Zavicefta® to patients who are on a controlled sodium diet.
Zavicefta may be diluted with sodium-containing solutions (see section 6.6) and this should be considered in relation to the total sodium from all sources that will be administered to the patient.
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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use, other beta-lactam antibacterials, third generation cephalosporins,ceftazidime, combinations, ATC code: J01DD52

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5.2 Pharmacokinetic properties

Distribution

The human protein binding of both ceftazidime and avibactam is approximately 10% and 8%, respectively. The steady-state volumes of distribution of ceftazidime and avibactam were about 17 L and 18 L, respectively in healthy adults following multiple doses of 2 g/0.5 g ceftazidime/avibactam infused over 2 hours every 8 hours. Both ceftazidime and avibactam penetrate into human bronchial epithelial lining fluid (ELF) to the same extent with concentrations around 30% of those in plasma. The concentration time profiles are similar for ELF and plasma.

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6. PHARMACEUTICAL PARTICULARS

6.2 Incompatibilities

The compatibility of Zavicefta with other medicines has not been established. Zavicefta should not be mixed with or physically added to solutions containing other medicinal products.
This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

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After dilution

Infusion bags

If the intravenous solution is prepared with diluents listed in section 6.6 (ceftazidime concentration 8 mg/mL), the chemical and physical in-use stability has been demonstrated (from initial vial puncture) for up to **12** hours at 2 - 8°C, followed by up to **4** hours at not more than 25ºC.
If the intravenous solution is prepared with diluents listed in section 6.6 (ceftazidime concentration > 8 mg/mL to 40 mg/mL), the chemical and physical in-use stability has been demonstrated (from initial vial puncture) for up to 4 hours at not more than 25°C. From a microbiological point of view, the medicinal product should be used immediately, unless reconstitution and dilution have taken place in controlled and validated aseptic conditions. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and must not exceed those stated above.

6.6 Special precautions for disposal and other handling

The powder must be reconstituted with water for injections and the resulting concentrate must then be immediately diluted prior to use. The reconstituted solution is pale yellow solution and free of particles.

Zavicefta (ceftazidime/avibactam) is a combination product; each vial contains 2 g of ceftazidime and 0.5 g of avibactam in a fixed 4:1 ratio. Dosage recommendations are based on the ceftazidime component only. Standard aseptic techniques should be used for solution preparation and administration. Doses may be prepared in an appropriately sized infusion bag.
Parenteral medicinal products should be inspected visually for particulate matter prior to administration.

Each vial is for single use only.

Any unused product or waste material should be disposed of in accordance with local requirements.

The total time interval between starting reconstitution and completing preparation of the intravenous infusion should not exceed 30 minutes.
Instructions for preparing adult in INFUSION BAG:

NOTE: The following procedure describes the steps to prepare an infusion solution with a final concentration of 8-40 mg/mL of ceftazidime. All calculations should be completed prior to initiating these steps.

1. Prepare the **reconstituted solution** (**167.3 mg/mL** of ceftazidime):

a) Insert the syringe needle through the vial closure and inject 10 mL of sterile water for injections.
b) Withdraw the needle and shake the vial to give a clear solution.
c) Insert a gas relief needle through the vial closure **after** the product has dissolved to relieve the internal pressure (this is important to preserve product sterility).

2. Prepare the **final solution** for infusion (final concentration must be **8-40 mg/mL** of ceftazidime):
Infusion bag: Further dilute the reconstituted solution by transferring an appropriately calculated volume of the reconstituted solution to an infusion bag containing any of the following: sodium chloride 9 mg/mL (0.9%) solution for injection, dextrose 50 mg/mL (5%) solution for injection, or Lactated Ringer's solution.

Refer to Table 7 below.

Table 7: Preparation of Zavicefta for adult in INFUSION BAG.

Zavicefta Dose (ceftazidime)[1]	**Volume to withdraw from reconstituted vial**	**Final volume after dilution in infusion bag[2]**
2 g	Entire contents (approximately 12 mL)	50 mL to 250 mL
1g	6 mL	25 mL to 125 mL
0.75 g	4.5 mL	19 mL to 93 mL
All other doses	Volume (mL) calculated based on dose required: **Dose (mg ceftazidime) ÷ 167.3 mg/mL ceftazidime**	Volume (mL) will vary based on infusion bag size availability and preferred final concentration (must be 8-40 mg/mL of ceftazidime)

[1] Based on ceftazidime component only.
[2] Dilute to final ceftazidime concentration of 8 mg/mL for in-use stability up to 12 hours at 2 - 8°C, followed by up to 4 hours at not more than 25°C (i.e. dilute 2 g dose of ceftazidime in 250 mL, 1 g dose of ceftazidime in 125 mL, 0.75 g dose of ceftazidime in 93 mL, etc.). All other ceftazidime concentrations (> 8 mg/mL to 40 mg/mL) have in-use stability up to 4 hours at not more than 25°C.

השינויים המודגשים ברקע צהוב מהווים החמרה. כמו כן, בוצעו שינויים נוספים הכוללים תוספת מידע, השמטת מידע ועדכוני נוסח שאינם מהווים החמרה. העלונים המעודכנים זמינים באתר משרד הבריאות.

https://israeldrugs.health.gov.il/#!/byDrug

לחילופין, לקבלת עלון מלא מודפס ניתן לפנות לחברת פייזר PFE פרמצבטיקה ישראל בע"מ, שנקר 9, ת.ד. 12133 הרצליה פיתוח, 46725.

בברכה,
עידית שלם אבידר
רוקחת ממונה

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