BioAvenir

02.22

רופא/ה, רוקח/ת נכבד/ה,

ברצוננו להודיעך על עדכון בעלונים של התכשירים :

AMPISULVENIR 1.5 G

אמפיסולבניר 1.5 גר'

AMPISULVENIR 3 G

אמפיסולבניר 3 גר'

המרכיבים הפעילים:

AMPISULVENIR 1.5 G:

AMPICILLIN (AS SODIUM SALT) 1000 MG

SULBACTAM (AS SODIUM SALT) 500 MG

AMPISULVENIR 3 G:

AMPICILLIN (AS SODIUM SALT) 2000 MG

SULBACTAM (AS SODIUM SALT) 1000 MG

צורת מינון:

POWDER FOR SOLUTION FOR INJECTION

התוויה:

Antibiotic for the treatment of bacterial infections caused by susceptible beta-lactamase producing strains of microorganisms, in the following conditions:

1. Skin and Skin Structure Infections ;

2. Intra- Abdominal Infections ;

3. Gynecological Infections .

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עדכונים מהותיים בעלון:

4.3 Contraindications

(…)

- Hypersensitivity (e.g., anaphylaxis or Stevens-Johnson syndrome) to ampicillin, sulbactam, or to other beta-lactam antibacterial drugs (e.g., penicillins and cephalosporins) or to any of the excipients
- AmpiSulVenir is contraindicated in patients with a previous history of cholestatic jaundice/hepatic dysfunction associated with AmpiSulVenir.

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4.4 Special warnings and precautions for use

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Hepatotoxicity

Hepatic dysfunction, including hepatitis and cholestatic jaundice has been associated with the use of AmpiSulVenir. Hepatic toxicity is usually reversible; however, deaths have been reported. Hepatic function should be monitored at regular intervals in patients with hepatic impairment.

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Severe Cutaneous Adverse Reactions

AmpiSulVenir may cause severe skin reactions, such as toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), dermatitis exfoliative, erythema multiforme, and Acute generalized exanthematous pustulosis (AGEP). If patients develop a skin rash they should be monitored closely and AmpiSulVenir discontinued if lesions progress (see **CONTRAINDICATIONS** and **ADVERSE REACTIONS** sections).

(…)

PRECAUTIONS

(…)

General:

Prescribing AmpiSulVenir in the absence of proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Information for Patients:

Patients should be counseled that antibacterial drugs including AmpiSulVenir should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When AmpiSulVenir is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by AmpiSulVenir or other antibacterial drugs in the future.

(…)

Diarrhea is a common problem caused by antibacterial which usually ends when the antibacterial is discontinued. Sometimes after starting treatment with antibacterial, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibacterial. If this occurs, patients should contact their physician as soon as possible.

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4.5 Interactions with other medicinal products and other forms of interaction

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Aminoglycosides

AmpiSulVenir and aminoglycosides should not be reconstituted together due to the *in vitro* inactivation of aminoglycosides by the ampicillin component of AmpiSulVenir.

(…)

Following administration of ampicillin to pregnant women, a transient decrease in plasma concentration of total conjugated estriol, estriol-glucuronide, conjugated estrone and estradiol has been noted. This effect may also occur with AmpiSulVenir.

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Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals have not been performed to evaluate carcinogenic or mutagenic potential.

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4.6 Pregnancy and lactation

Pregnancy

Reproduction studies have been performed in mice, rats, and rabbits at doses up to ten (10) times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Ampicillin and Sulbactam. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response,

Labor and Delivery:

Studies in guinea pigs have shown that intravenous administration of ampicillin decreased the uterine tone, frequency of contractions, height of contractions, and duration of

contractions. However, it is not known whether the use of Ampicillin and Sulbactam in humans during labor or delivery has immediate or delayed adverse effects on the fetus, prolongs the duration of labor, or increases the likelihood that forceps delivery or other obstetrical intervention or resuscitation of the newborn will be necessary.

Nursing Mothers: Low concentrations of ampicillin and sulbactam are excreted in the milk; therefore, caution should be exercised when AmpiSulVenir is administered to a nursing woman.

Pediatric Use: The safety and effectiveness of ampicillin and sulbactam have been established for pediatric patients one year of age and older for skin and skin structure infections as approved in adults. Use of ampicillin and sulbactam in pediatric patients is supported by evidence from adequate and well-controlled studies in adults with additional data from pediatric pharmacokinetic studies, a controlled clinical trial conducted in pediatric patients and post-marketing adverse events surveillance.

The safety and effectiveness of ampicillin and sulbactam have not been established for pediatric patients for intra-abdominal infections.

4.8 Undesirable effects

(…)

Adult Patients: ampicillin and sulbactam is generally well tolerated. The following adverse reactions have been reported in clinical trials.

Local Adverse Reactions

Pain at IM injection site – 16%

Pain at IV injection site – 3%

Thrombophlebitis – 3%

Phlebitis – 1.2%

Systemic Adverse Reactions

The most frequently reported adverse reactions were diarrhea in 3% of the patients and rash in less than 2% of the patients

Additional systemic reactions reported in less than 1% of the patients were: itching, nausea, vomiting, candidiasis, fatigue, malaise, headache, chest pain, flatulence, abdominal distension, glossitis, urine retention, dysuria, edema, facial swelling, erythema, chills, tightness in throat, substernal pain, epistaxis and mucosal bleeding.

Pediatric Patients: Available safety data for pediatric patients treated with ampicillin and sulbactam demonstrate a similar adverse events profile to those observed in adult patients.

Additionally, atypical lymphocytosis has been observed in one pediatric patient receiving ampicillin and sulbactam.

Adverse Laboratory Changes

Adverse laboratory changes without regard to drug relationship that were reported during clinical trials were:

Hepatic: Increased AST (SGOT), ALT (SGPT), alkaline phosphatase, and LDH.

Hematologic: Decreased hemoglobin, hematocrit, RBC, WBC, neutrophils, lymphocytes, platelets and increased lymphocytes, monocytes, basophils, eosinophils, and platelets.

Blood Chemistry: Decreased serum albumin and total proteins.

Renal: Increased BUN and creatinine.

Urinalysis: Presence of RBC's and hyaline casts in urine.

Postmarketing Experience

In addition to adverse reactions reported from clinical trials, the following have been identified during post-marketing use of ampicillin sodium/sulbactam sodium or other products containing ampicillin. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. These events have been chosen for inclusion due to a combination of their seriousness, frequency, or potential causal connection to ampicillin sodium/sulbactam sodium.

Blood and Lymphatic System Disorders: Hemolytic anemia, thrombocytopenic purpura and agranulocytosis have been reported. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. Some individuals have developed positive direct Coombs Tests during treatment with ampicillin and sulbactam , as with other beta-lactam antibacterials.

Gastrointestinal Disorders: Abdominal pain, cholestatic hepatitis, cholestasis, hyperbilirubinemia, jaundice, abnormal hepatic function, melena, gastritis, stomatitis, dyspepsia, black "hairy" tongue and *Clostridium difficile* associated diarrhea (see CONTRAINDICATIONS and WARNINGS sections).

General Disorders and Administration Site Conditions: injection site reaction

Immune System Disorders*:* Serious and fatal hypersensitivity (anaphylactic) reactions (see WARNINGS section), Acute myocardial ischemia with or without myocardial infarction may occur as part of an allergic reaction.

Nervous System Disorders: Convulsion and dizziness

Renal and Urinary Disorders: Tubulointerstitial nephritis

Respiratory, Thoracic and Mediastinal Disorders: Dyspnea

Skin and Subcutaneous Tissue Disorders: Toxic epidermal necrolysis, Stevens-Johnson syndrome, angioedema, Acute generalized exanthematous pustulosis (AGEP), erythema multiforme, exfoliative dermatitis and urticaria (see **CONTRAINDICATIONS** and **WARNINGS** sections).

4.9 Overdose

Neurological adverse reactions, including convulsions, may occur with the attainment of high CSF levels of beta-lactams. Ampicillin may be removed from circulation by hemodialysis. The molecular weight, degree of protein binding and pharmacokinetics profile of sulbactam suggest that this compound may also be removed by hemodialysis.

5. PHARMACOLOGICAL PROPERTIES

ראה עדכונים בעלון המצורף

לתשומת לב - בהודעה זו מצוינים שינויים מהותיים והחמרות. בעלון בוצעו שינויים נוספים.
יש לעיין בעלון המצורף לאריזה (ולהודעה זו) לפני השימוש בתכשירים .

העלון נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלו מודפס ע"י פניה לבעל הרישום ביואבניר בע"מ , דוד המלך 1 הרצליה פיתוח או בטלפון 09-9544129.

בכבוד רב,

שרית קיראי-קוצ'וק

רוקחת ממונה