הודעה על החמרה (מידע בטיחות) בעלון לרופא

(מעודכן 3102.50)

תאריך 08.12.2013

שם תכשיר באנגלית ומספר הרישום

UNASYN 0.75GR 122.44.30257.00

UNASYN 1.5GR 122.47.30258.00

UNASYN 3.0GR 122.48.30259.00

שם בעל הרישום פייזר פרמצבטיקה ישראל בע"מ

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות

פרק בעלון	טקסט נוכחי	טקסט חדש
Indication		To reduce the development of drug-resistant bacteria and maintain effectiveness of UNASYN and other antibacterial drugs, UNASYN should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.
Description	Unasyn is available as a dry powder for reconstitution in vials containing the equivalent of 1,000mg + 2,000mg, 500mg + 1,000mg, 250mg + 500mg of sulbactam and ampicillin, respectively.	~~Unasyn is available as a dry powder for reconstitution in vials containing the equivalent of 1,000mg + 2,000mg, 500mg + 1,000mg, 250mg + 500mg of sulbactam and ampicillin, respectively.~~ 1.5 g of UNASYN (1 g ampicillin as the sodium salt plus 0.5 g sulbactam as the sodium salt) parenteral contains approximately 115 mg (5 mEq) of sodium. 3 g of UNASYN (2 g ampicillin as the sodium salt plus 1 g sulbactam as the sodium salt) parenteral contains approximately 230 mg (10 mEq) of sodium
Microbiology	Recommended ampicillin/sulbactam, Susceptibility Ranges: Resistant: MIC (mcg of ampicillin/mL) > 4 Intermediate: --- Susceptible: ≤2	Recommended ampicillin/sulbactam, Susceptibility Ranges: Resistant: MIC (mcg of ampicillin/mL) > 4 Intermediate: --- Susceptible: ≤2
Contraindications		

For IV administration, the dose can be given by slow intravenous injection over at least 10–15 minutes or can also be delivered in greater dilutions with 50–100 mL of a compatible diluent as an intravenous infusion over 15–30 minutes. UNASYN may be administered by deep intramuscular injection. (see **DIRECTIONS FOR USE-Preparation for Intramuscular Injection** section). The recommended adult dosage of UNASYN is 1.5 g (1 g ampicillin as the sodium salt plus 0.5 g sulbactam as the sodium salt) to 3 g (2 g ampicillin as the sodium salt plus 1 g sulbactam as the sodium salt) every six hours. This 1.5 to 3 g range represents the total of ampicillin content plus the sulbactam content of UNASYN, and corresponds to a range of 1 g ampicillin/0.5 g sulbactam to 2 g ampicillin/1 g sulbactam. The total dose of sulbactam should not exceed 4 grams per day. ~~The following dilutions may be used:~~ ~~Total Package Dosage (g) Equivalent Diluent Dosage of Sulbactam-Ampicillin (g) Maximum Final~~ ~~1. 0.375 0.125 - 0.25 10 ml vial 0.8 125 - 250~~ ~~2. 0.75 0.25 - 0.5 10 ml vial 1.6 125 - 250~~ ~~3. 1.5 0.5 - 1.0 20 ml vial 3.2 125 - 250~~ ~~4. 3.0 1.0 - 2.0 20 ml vial 6.4 125 - 250~~ ~~5. 0.75 0.25 - 0.5 100 ml PBU 25 10 - 20~~ ~~6. 1.5 0.5 - 1.0 100 ml PBU 50 10 - 20~~ ~~7. 3.0 1.0 - 2.0 100 ml PBU 100 10 - 20~~ ~~PBU = piggyback unit~~ ~~For intravenous administration, sulbactam sodium/ampicillin sodium IM/IV should be reconstituted with sterile water for injection or any compatible solution. (See section 6.6 - Instructions for Use.) To ensure complete dissolution, allow foaming to dissipate in order to visually inspect. The dose can be given by bolus injection over a~~	The following dilutions may be used: Total Dosage (g) Equivalent Dosage of Sulbactam-Ampicillin (g) 1. 0.375 0.125 - 0.25 2. 0.75 0.25 - 0.5 3. 1.5 0.5 - 1.0 4. 3.0 1.0 - 2.0 5. 0.75 0.25 - 0.5 6. 1.5 0.5 - 1.0 7. 3.0 1.0 - 2.0 PBU = piggyback unit For intravenous administration, sulbactam sodium/ampicillin sodium IM/IV should be reconstituted with sterile water for injection or any compatible solution. (See section 6.6 - Instructions for Use.) To ensure complete dissolution, allow foaming to dissipate in order to visually inspect. The dose can be given by bolus injection over a minimum of 3 minutes or can be used in greater dilutions as an intravenous infusion over 15-30 minutes UNASYN may be administered by deep intramuscular injection. (See Preparation for Intramuscular Injection.) if pain is experienced, 0.5% sterile solution for injection of lignocaine hydrochloride anhydrous may be used for reconstitution of the powder. Use in Adults The usual dosage range of sulbactam sodium/ampicillin sodium IM/IV is 1.5 g to 12 g per day in divided doses every 6 or 8 hours up to a maximum daily dosage of sulbactam of 4 g. Less severe infections may be treated on an every-12-hours schedule. SEVERITY OF INFECTION DAILY DOSE OF sulbactam sodium/ampicillin sodium IM/IV (g)	**Posology, dosage & administration**

~~minimum of 3 minutes or can be used in greater dilutions as an intravenous infusion over 15-30 minutes~~ ~~UNASYN may be administered by deep intramuscular injection. (See Preparation for Intramuscular Injection.) if pain is experienced, 0.5% sterile solution for injection of lignocaine hydrochloride anhydrous may be used for reconstitution of the powder.~~ ~~Use in Adults~~ ~~The usual dosage range of sulbactam sodium/ampicillin sodium IM/IV is 1.5 g to 12 g per day in divided doses every 6 or 8 hours up to a maximum daily dosage of sulbactam of 4 g. Less severe infections may be treated on an every-12-hours schedule.~~ ~~SEVERITY OF INFECTION~~ ~~DAILY DOSE OF sulbactam sodium/ampicillin sodium IM/IV (g)~~ ~~Mild 1.5 to 3 (0.5 + 1 to 1 + 2)~~ ~~Moderate up to 6 (2 + 4)~~ ~~Severe up to 12 (4 + 8)~~ ~~More or less frequent dosing may be indicated depending on the severity of the illness and the renal function of the patient. Treatment is usually continued until 48 hours after pyrexia and other abnormal signs have resolved. Treatment is normally given for 5 to 14 days, but the treatment period may be extended or additional ampicillin may be administered in severely ill cases.~~ ~~In treating patients on restricted sodium intake, it should be noted that 1,500 mg of sulbactam sodium/ampicillin sodium IM/IV contains approximately 115 mg (5 mmol) of sodium.~~ ~~For the prophylaxis of surgical infections, 1.5-3 g of sulbactam sodium/ampicillin sodium IM/IV should be given at induction of anesthesia, which allows sufficient time to achieve effective serum and tissue concentrations during the procedure. The dose may be repeated every 6-8 hours; administration is usually stopped 24 hours after the majority of surgical procedures, unless a therapeutic course of sulbactam sodium/ampicillin sodium IM/IV is~~	Mild 1.5 to 3 (0.5 + 1 to 1 + 2) Moderate up to 6 (2 + 4) Severe up to 12 (4 + 8) More or less frequent dosing may be indicated depending on the severity of the illness and the renal function of the patient. Treatment is usually continued until 48 hours after pyrexia and other abnormal signs have resolved. Treatment is normally given for 5 to 14 days, but the treatment period may be extended or additional ampicillin may be administered in severely ill cases. In treating patients on restricted sodium intake, it should be noted that 1,500 mg of sulbactam sodium/ampicillin sodium IM/IV contains approximately 115 mg (5 mmol) of sodium. For the prophylaxis of surgical infections, 1.5-3 g of sulbactam sodium/ampicillin sodium IM/IV should be given at induction of anesthesia, which allows sufficient time to achieve effective serum and tissue concentrations during the procedure. The dose may be repeated every 6-8 hours; administration is usually stopped 24 hours after the majority of surgical procedures, unless a therapeutic course of sulbactam sodium/ampicillin sodium IM/IV is indicated. In the treatment of uncomplicated gonorrhea, sulbactam sodium/ampicillin sodium IM/IV can be given as a single dose of 1.5 g. Concomitant probenecid 1.0 g orally should be administered in order to prolong plasma concentrations of sulbactam and ampicillin. **Use in Children, Infants and Neonates** The dosage of sulbactam sodium/ampicillin sodium IM/IV for most infections in children,	

~~indicated.~~ ~~In the treatment of uncomplicated gonorrhea, sulbactam sodium/ampicillin sodium IM/IV can be given as a single dose of 1.5 g. Concomitant probenecid 1.0 g orally should be administered in order to prolong plasma concentrations of sulbactam and ampicillin.~~ ~~**Use in Children, Infants and Neonates**~~ ~~The dosage of sulbactam sodium/ampicillin sodium IM/IV for most infections in children, infants and neonates is 150 mg/kg/day (corresponding to sulbactam 50 mg/kg/day and ampicillin 100 mg/kg/day).~~ ~~In children, infants and neonates, dosing is usually every 6 or 8 hours in accordance with the usual practice for ampicillin.~~ ~~In neonates during the first week of life (especially preterms), the recommended dose is 75 mg/kg/day (corresponding to 25 mg/kg/day sulbactam and 50 mg/kg/day ampicillin) in divided doses every 12 hours.~~ **Pediatric Patients 1 Year of Age or Older:** The recommended daily dose of UNASYN in pediatric patients is 300 mg per kg of body weight administered via intravenous infusion in equally divided doses every 6 hours. This 300 mg/kg/day dosage represents the total ampicillin content plus the sulbactam content of UNASYN, and corresponds to 200 mg ampicillin/100 mg sulbactam per kg per day. The safety and efficacy of UNASYN administered via intramuscular injection in pediatric patients have not been established. Pediatric patients weighing 40 kg or more should be dosed according to adult recommendations, and the total dose of sulbactam should not exceed 4 grams per day. The course of intravenous therapy should not routinely exceed 14 days. In clinical trials, most children received a course of oral antimicrobials following initial treatment with intravenous UNASYN. (see **CLINICAL STUDIES** section).	infants and neonates is 150 mg/kg/day (corresponding to sulbactam 50 mg/kg/day and ampicillin 100 mg/kg/day). In children, infants and neonates, dosing is usually every 6 or 8 hours in accordance with the usual practice for ampicillin. In neonates during the first week of life (especially preterms), the recommended dose is 75 mg/kg/day (corresponding to 25 mg/kg/day sulbactam and 50 mg/kg/day ampicillin) in divided doses every 12 hours.	
If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be	…. Since infectious mononucleosis is viral in origin, sulbactam sodium/ampicillin sodium IM/IV should not be used in its treatment. A high percentage of patients with	**Special Warnings and Special Precautions for Use**

instituted as clinically indicated. … ~~Since infectious mononucleosis is viral in origin, sulbactam sodium/ampicillin sodium IM/IV should not be used in its treatment. A high percentage of patients with mononucleosis who received ampicillin have developed a skin rash.~~ **General:** A high percentage of patients with mononucleosis who received ampicillin have developed a skin rash. Thus, ampicillin class antibiotics should not be administered to patients with mononucleosis. In patients treated with UNASYN the possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur (usually involving *Pseudomonas* or *Candida*), the drug should be discontinued and/or appropriate therapy instituted. Prescribing UNASYN 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 UNASYN should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When UNASYN 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 UNASYN or other antibacterial drugs in the future. Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, 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 antibiotic. If this occurs, patients should contact their physician as soon as possible.	mononucleosis who received ampicillin have developed a skin rash.	

UNASYN and aminoglycosides should not be reconstituted together due to the *in vitro* inactivation of aminoglycosides by the ampicillin component of UNASYN		**Interaction with Other Medicaments and Other Forms of Interaction**
Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. (see –**PRECAUTIONS-Drug/Laboratory Test Interactions** section).		**Fertility, Pregnancy and Lactation**
The following adverse reactions have been identified in post-marketing reports: Hepatitis cholestatic and cholestasis.		**Adverse events**
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 ~~Limited information is available on the acute toxicity of ampicillin sodium and sulbactam sodium in humans. Overdosage of the drug would be expected to produce manifestations that are principally extensions of the adverse reactions reported with the drug. The fact that high CSF concentrations of β-lactam antibiotics may cause neurologic effects, including seizures, should be considered. Because ampicillin and sulbactam are both removed from the circulation by hemodialysis, these procedures may enhance elimination of the drug from the body if overdosage occurs in patients with impaired renal function~~	Limited information is available on the acute toxicity of ampicillin sodium and sulbactam sodium in humans. Overdosage of the drug would be expected to produce manifestations that are principally extensions of the adverse reactions reported with the drug. The fact that high CSF concentrations of β-lactam antibiotics may cause neurologic effects, including seizures, should be considered. Because ampicillin and sulbactam are both removed from the circulation by hemodialysis, these procedures may enhance elimination of the drug from the body if overdosage occurs in patients with impaired renal function	**Overdosage**