For Medical Professional only

Ambac

0.75g Injection
1.5g Injection

(Ampicillin + Sulbactam Injection U.S.P.)
(Product Specs.: U.S.P.)

ایم بیک انجکشن

DESCRIPTION:
AMBAC is an injectable antibacterial combination consisting of the semisynthetic antibacterial ampicillin sodium and the beta-lactamase inhibitor sulbactam sodium for intravenous and intramuscular administration.

Ampicillin sodium is derived from the penicillin nucleus, 6-aminopenicillanic acid. Chemically, it is monosodium (2S, 5R, 6R)-6-[(R)-2-amino-2-phenylacetamido]-3, 3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylate and has a molecular weight of 371.39. Its chemical formula is C16H18N3NaO4S.

Sulbactam sodium is a derivative of the basic penicillin nucleus. Chemically, sulbactam sodium is sodium penicillinate sulfone; sodium (2S, 5R)-3,3-dimethyl-7-oxo-4-thia- 1-azabicyclo [3.2.0] heptane-2-carboxylate 4,4-dioxide. Its chemical formula is C8H10NNaO5S with a molecular weight of 255.22.

AMBAC, ampicillin sodium/sulbactam sodium parenteral combination, is available as a white to off-white dry powder for reconstitution. AMBAC dry powder is freely soluble in aqueous diluents to yield pale yellow to yellow solutions containing ampicillin sodium and sulbactam sodium equivalent to 250 mg ampicillin per mL and 125 mg sulbactam per mL. The pH of the solutions is between 8.0 and 10.0. Dilute solutions (up to 30 mg ampicillin and 15 mg sulbactam per mL) are essentially colorless to pale yellow. The pH of dilute solutions remains the same.

Ambac brand of ampicillin sodium/ sulbactam sodium combincation available as a dry powder for reconstitution, in vial containing the equivalent of 500mg ampicillin sodium and 250mg sulbactam sodium and 1000 mg ampicillin sodium and 500 mg sulbactam sodium.

CLINICAL PHARMACOLOGY:
GENERAL:
Immediately after completion of a 15-minute intravenous infusion of AMBAC, peak serum concentrations of ampicillin and sulbactam are attained. Ampicillin serum levels are similar to those produced by the administration of equivalent amounts of ampicillin alone. Peak ampicillin serum levels ranging from 109 to 150 mcg/mL are attained after administration of 2000 mg of ampicillin plus 1000 mg sulbactam and 40 to 71 mcg/mL after administration of 1000 mg ampicillin plus 500 mg sulbactam. The corresponding mean peak serum levels for sulbactam range from 48 to 88 mcg/mL and 21 to 40 mcg/mL, respectively. After an intramuscular injection of 1000 mg ampicillin plus 500 mg sulbactam, peak ampicillin serum levels ranging from 8 to 37 mcg/mL and peak sulbactam serum levels ranging from 6 to 24 mcg/mL are attained.

The mean serum half-life of both drugs is approximately 1 hour in healthy volunteers.
Approximately 75 to 85% of both ampicillin and sulbactam are excreted unchanged in the urine during the first 8 hours after administration of AMBAC to individuals with normal renal function. Somewhat higher and more prolonged serum levels of ampicillin and sulbactam can be achieved with the concurrent administration of probenecid.

In patients with impaired renal function the elimination kinetics of ampicillin and sulbactam are similarly affected, hence the ratio of one to the other will remain constant whatever the renal function. The dose of AMBAC in such patients should be administered less frequently in accordance with the usual practice for ampicillin Ampicillin has been found to be approximately 28% reversibly bound to human serum protein and sulbactam approximately 38% reversibly bound.

Penetration of both ampicillin and sulbactam into cerebrospinal fluid in the presence of inflamed meninges has been demonstrated after IV administration of AMBAC.

The pharmacokinetics of ampicillin and sulbactam in pediatric patients receiving AMBAC are similar to those observed in adults. Immediately after a 15-minute infusion of 50 to 75 mg AMBAC/kg body weight, peak serum and plasma concentrations of 82 to 446 mcg ampicillin/mL and 44 to 203 mcg sulbactam/mL were obtained. Mean half-life values were approximately 1 hour.

MICROBIOLOGY
Ampicillin is similar to benzyl penicillin in its bactericidal action against susceptible organisms during the stage of active multiplication. It acts through the inhibition of cell wall mucopeptide biosynthesis. Ampicillin has a broad spectrum of bactericidal activity against many gram-positive and gram-negative aerobic and anaerobic bacteria. (Ampicillin is,

however, degraded by beta-lactamases and therefore the spectrum of activity does not normally include organisms which produce these enzymes).

The presence of sulbactam in the AMBAC formulation effectively extends the antibacterial spectrum of ampicillin to include many bacteria normally resistant to it and to other beta-lactam antibacterials. Thus, AMBAC possesses the properties of a broad-spectrum antibacterial and a beta-lactamase inhibitor.

While in vitro studies have demonstrated the susceptibility of most strains of the following organisms, clinical efficacy for infections other than those included in the INDICATIONS and USAGE section has not been documented.

Gram-Positive Bacteria: Staphylococcus aureus (beta-lactamase and non-beta-lactamase producing), Staphylococcus epidermidis (beta-lactamase and non-beta-lactamase producing), Staphylococcus saprophyticus (beta-lactamase and non-beta-lactamase producing), Streptococcus faecalis† (Enterococcus), Streptococcus pneumoniae† (formerly D. pneumoniae), Streptococcus pyogenes† , Streptococcus viridans† .

Gram-Negative Bacteria: Hemophilus influenzae (beta-lactamase and non-beta-lactamase producing), Moraxella (Branhamella) catarrhalis (beta-lactamase and non-beta-lactamase producing), Escherichia coli (beta-lactamase and non-beta-lactamase producing), Klebsiella species (all known strains are beta-lactamase producing), Proteus mirabilis (beta-lactamase and non-beta-lactamase producing), Proteus vulgaris, Providencia rettgeri, Providencia stuartii, Morganella morganii, and Neisseria gonorrhoeae (beta-lactamase and non-beta-lactamase producing).

Anaerobes: Clostridium species, † Peptococcus species, † Peptostreptococcus species, Bacteroides species, including B. fragilis. These are not beta-lactamase producing strains and, therefore, are susceptible to ampicillin alone.

THERAPEUTIC INDICATIONS:
AMBAC is indicated for the treatment of infections due to susceptible strains of the designated microorganisms in the conditions listed below.
Skin and Skin Structure Infections caused by beta-lactamase producing strains of Staphylococcus aureus, Escherichia coli,* Klebsiella spp.* (including K. pneumoniae*), Proteus mirabilis,* Bacteroides fragilis,* Enterobacter spp.,* and Acinetobacter calcoaceticus.

Intra-Abdominal Infections caused by beta-lactamase producing strains of Escherichia coli, Klebsiella spp. (including K. pneumoniae*), Bacteroides spp. (including B. fragilis), and Enterobacter spp.

Gynecological Infections caused by beta-lactamase producing strains of Escherichia coli,* and Bacteroides spp.* (including B. fragilis*).

While AMBAC is indicated only for the conditions listed above, infections caused by ampicillin-susceptible organisms are also amenable to treatment with AMBAC due to its ampicillin content. Therefore, mixed infections caused by ampicillin-susceptible organisms and beta-lactamase producing organisms susceptible to AMBAC should not require the addition of another antibacterial.

Appropriate culture and susceptibility tests should be performed before treatment in order to isolate and identify the organisms causing infection and to determine their susceptibility to AMBAC.

To reduce the development of drug-resistant bacteria and maintain effectiveness of AMBAC and other antibacterial drugs, AMBAC should be used only to treat 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.

DOSAGE:
ADULT DOSAGE:
The recommended adult dosage of AMBAC 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 AMBAC, 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.

Pediatric Patients 1 Year of Age or Older: The recommended daily dose of AMBAC 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 AMBAC, and corresponds to 200 mg ampicillin/100 mg sulbactam per kg per day. The safety and efficacy of AMBAC 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.

Impaired Renal Function
In patients with impairment of renal function the elimination kinetics of ampicillin and sulbactam are similarly affected, hence the ratio of one to the other will remain constant whatever the renal function. The dose of AMBAC in such patients should be administered less frequently in accordance with the usual practice for ampicillin and according to the following recommendations:

Creatinine Clearance (mL/min/1.73m2)	Ampicillin/Sulbactam Half-Life (Hours)	Recommended AMBAC Dosage
≥30	1	1.5–3 g q 6h-q 8h
15–29	5	1.5–3 g q 12h
5–14	9	1.5–3 g q 24h

CONTRAINDICATIONS:
The use of AMBAC is contraindicated in individuals with a history of serious hypersensitivity reactions (e.g., anaphylaxis or Stevens-Johnson syndrome) to ampicillin, sulbactam or to other beta-lactam

antibacterial drugs (e.g., penicillins and cephalosporins).
AMBAC is contraindicated in patients with a previous history of cholestatic jaundice/hepatic dysfunction associated with AMBAC.

METHOD OF ADMINISTRATION:
AMBAC may be administered by either the IV or the IM routes.
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. AMBAC may be administered by deep intramuscular injection.

ADVERSE EFFECTS:
Ambac is generally well tolerated. The majority of side effects observed were of mild or moderate severity and were normally tolerated with continued treatment.

Infections and Infestations: Pseudomembraneous colitis.
Immune System Disorders: Anaphylactic shock, anaphylactic reaction, hypersensitivity.
Nervous System Disorders: Dizziness, somnolence, sedation, headache.
Respiratory, Thoracic and Mediastinal Disorders: Dyspnoea.
Gastrointestinal Disorders: Enterocolitis, melaena, diarrhoea, vomiting, abdominal pain, dyspepsia, nausea.
Skin and Subcutaneous Tissue Disorders: Angioedema, urticaria, dermatitis, rash, pruritus.
General Disorders and Administration Site Conditions: Fatigue, malaise.
Adverse reactions associated with the use of ampicillin alone may be observed with Ambac.
Adverse reactions associated with the use of ampicillin and/or sulbactam/ampicillin IM/IV include:
Blood and Lymphatic System Disorders: Agranulocytosis, hemolytic anaemia, thrombocytopenic purpura, thrombocytopenia, leukopenia, neutropenia, eosinophilia, anaemia.
Nervous System Disorders: Convulsion.
Gastrointestinal Disorders: Glossitis, stomatitis, tongue discolouration.
Hepatobiliary Disorders: Cholestasis, cholestasis hepatic, bilirubinaemia, hepatic function abnormal, jaundice.
Skin and Subcutaneous Tissue Disorders: Toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, dermatitis exfoliative.
Renal and Urinary Disorders: Tubulointerstitial nephritis.

PRECAUTIONS & WARNING:
General: A high percentage of patients with mononucleosis who receive ampicillin develop a skin rash. Thus, ampicillin class antibacterial should not be administered to patients with mononucleosis. In patients treated with AMBAC 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 AMBAC 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.

Hypersensitivity
Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. These reactions are more apt to occur in individuals with a history of penicillin hypersensitivity and/or hypersensitivity reactions to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe reactions when treated with cephalosporins. Before therapy with a penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, and other allergens. If an allergic reaction occurs, AMBAC should be discontinued and the appropriate therapy instituted.

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

Severe Cutaneous Reactions
AMBAC may cause severe skin reactions, such as toxic epidermal necrolysis (TEN), StevensJohnson syndrome (SJS), dermatitis exfoliative, erythema multiforme, and Acute generalized exanthematous pustulosis (AGEP). If patients develop a skin rash they should be monitored closely and AMBAC discontinued if lesions progress.

Clostridium difficile-Associated Diarrhea
Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including AMBAC, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibacterial drug use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibacterial drug use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibacterial treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

USE IN PREGNANCY AND BREAST-FEEDING:
Pregnancy
Pregnancy Category: B
However, safety for use in human pregnancy has not been established. Therefore, Ambac should be used during pregnancy only if the potential benefits outweigh the potential risk.

Breast-feeding
Low concentrations of ampicillin and sulbactam are excreted in the milk; therefore, caution should be exercised when AMBAC is administered to a nursing woman.

DRUG INTERACTIONS:
Probenecid decreases the renal tubular secretion of ampicillin and sulbactam. Concurrent use of probenecid with AMBAC may result in increased and prolonged blood levels of ampicillin and sulbactam. The concurrent administration of allopurinol and ampicillin increases substantially the incidence of rashes in patients receiving both drugs as compared to patients receiving ampicillin alone. It is not known whether this potentiation of ampicillin rashes is due to allopurinol or the hyperuricemia present in these patients. There are no data with AMBAC and allopurinol administered concurrently. AMBAC and aminoglycosides should not be reconstituted together due to the in vitro inactivation of aminoglycosides by the ampicillin component of AMBAC.

OVERDOSAGE:
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.

COMPATIBILITY AND STABILITY:
AMBAC sterile powder is to be stored below 30°C (86°F) prior to reconstitution.
When concomitant therapy with aminoglycosides is indicated, AMBAC and aminoglycosides should be reconstituted and administered separately, due to the in vitro inactivation of aminoglycosides by any of the aminopenicillins.
Solutions should be allowed to stand after dissolution to allow any foaming to dissipate in order to permit visual inspection for complete solubilization.

PRESENTATION:
Ambac (ampicillin sodium / sulbactam sodium) is supplied as a sterile off-while dry powder in glass vials. The following packages are available.
Ambac vials containing 0.75g IV/IM (0.5g ampicillin sodium 0.25g sulbactam sodium)
Ambac vials containing 1.5g IV/IM (1g ampicillin sodium 0.5g sulbactam sodium)

DIRECTIONS:
- Protect from light & moisture, store below 30ºC.
- Keep out of the reach of children, use as directed by physician.
- For suspected adverse drug reaction for BOSCH products, report at ade@bosch-pharma.com

WARNING:
To be sold on the prescription of registered medical practitioner only.

خوراک اور ترکیب استعمال:
ایم بیک:
بالغ افراد اور 12 سال سے زائد عمر کے بچوں کے لئے:
عمومی خوراک:۔ ایم بیک انجکشن 1.5 گرام ہر 6 گھنٹوں کے وقفوں میں دی جائے۔
نوٹ:۔ سالبیکٹم کی کل مقدار 4 گرام یومیہ سے تجاوز نہ کرے۔
ایک سال اور ایک سال سے زیادہ عمر کے بچوں کے لئے:
عمومی خوراک:۔ ایم بیک انجکشن 300 ملی گرام فی کلوگرام جسمانی وزن روزانہ کے حساب سے مساوی مقدار میں تقسیم کر کے 6 گھنٹوں کے وقفوں سے دی جائے۔
نوٹ:۔ سالبیکٹم کی کل مقدار 4 گرام یومیہ سے تجاوز نہ کرے۔
ایم بیک ہیٹن اور یدی مقدار آہستہ آہستہ 10 سے 15 منٹ کے درمیان دی جاسکتی ہے یا چھوٹی کثیر المقدار 50 سے 100 ملی گرام ڈائیلوینٹ کے ساتھ 15 سے 30 منٹ میں بھی دی جاسکتی ہے۔

ہدایات:
روشنی اور نمی سے محفوظ کمرے کے درجہ حرارت (۳۰ ڈگری سینٹی گریڈ سے کم) پر رکھیں۔
بچوں کی پہنچ سے دور رکھیں۔
ڈاکٹری ہدایت کے مطابق استعمال کریں۔
انتباہ: صرف رجسٹرڈ میڈیکل پریکٹیشنر کے نسخے پر فروخت کے لئے۔

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ISO 9001:2015 Certified Company