**INDICATIONS AND USAGE**
ZOSYN is a combination penicillin-class antibacterial and β-lactamase inhibitor indicated for treatment of:
- Intra-abdominal infections (1.1)
- Skin and skin structure infections (1.2)
- Female pelvic infections (1.3)
- Community-acquired pneumonia (1.4)
- Nosocomial pneumonia (1.5)
- Usage (1.6)

To reduce the development of drug-resistant bacteria and maintain the effectiveness of ZOSYN and other antibacterial drugs, ZOSYN should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

**DOSAGE AND ADMINISTRATION**
- The usual daily dose of ZOSYN for adults is 3.375 g every six hours totaling 13.5 g (12.0 g piperacillin/1.5 g tazobactam). (2.1)
- Initial presumptive treatment of patients with nosocomial pneumonia should start with ZOSYN at a dosage of 4.5 g every six hours plus an aminoglycoside, totaling 18.0 g (16.0 g piperacillin/2.0 g tazobactam). (2.2)
- Dosage in patients with renal impairment (≤40 mL/min of CRCL) and dialysis patients should be reduced, based on the degree of actual renal function impairment. (2.3)
- For children with appendicitis and/or peritonitis the recommended ZOSYN dosage is 100 mg piperacillin/12.5 mg tazobactam per kilogram of body weight, every 8 hours in pediatric patients 9 months of age and older. For pediatric patients 2 to 9 months of age, the recommended dosage is 80 mg piperacillin/10 mg tazobactam per kilogram of body weight, every 8 hours. (2.4)
- ZOSYN and aminoglycosides should be reconstituted, diluted, and administered separately. Co-administration via Y-site can be done under certain conditions. (2.7)

**DOSAGE FORMS AND STRENGTHS**
- ZOSYN® for Injection: 2.25 g, 3.375 g, and 4.5 g lyophilized powder for reconstitution in single-dose vials and 40.5 g lyophilized powder for reconstitution in pharmacy bulk vials. (3)
- ZOSYN® Injection: 2.25 g in 50 mL, 3.375 g in 50 mL, and 4.5 g in 100 mL frozen solution in single-dose GALAXY containers. (3, 16)

**CONTRAINDICATIONS**
Patients with a history of allergic reactions to any of the penicillins, cephalosporins, or β-lactamase inhibitors. (4)

**WARNINGS AND PRECAUTIONS**
- Serious hypersensitivity reactions (anaphylactic/anaphylactoid) reactions have been reported in patients receiving ZOSYN. Discontinue ZOSYN if a reaction occurs. (5.1)
- ZOSYN may cause severe cutaneous adverse reactions, such as Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, and acute generalized exanthematous pustulosis (5.2). Discontinue ZOSYN for progressive rashes.
- Hematological effects (including bleeding, leukopenia and neutropenia) have occurred. Monitor hematologic tests during prolonged therapy. (5.3)
- Nephrotoxicity in critically ill patients has been observed; the use of ZOSYN was found to be an independent risk factor for renal failure and was associated with delayed recovery of renal function as compared to other beta-lactam antibacterials. (5.5)
antibacterial drugs in a randomized, multicenter, controlled trial in critically ill patients. Based on this study, alternative treatment options should be considered in the critically ill population. If alternative treatment options are inadequate or unavailable, monitor renal function during treatment with ZOSYN. (5.5)

- *Clostridium difficile* associated diarrhea: evaluate patients if diarrhea occurs. (5.7)

### ADVERSE REACTIONS

The most common adverse reactions (incidence >5%) are diarrhea, constipation, nausea, headache and insomnia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

### DRUG INTERACTIONS

- ZOSYN administration can significantly reduce tobramycin concentrations in hemodialysis patients. Monitor tobramycin concentrations in these patients. (7.1)
- Probenecid prolongs the half-lives of piperacillin and tazobactam and should not be co-administered with ZOSYN unless the benefit outweighs the risk. (7.2)
- Co-administration of ZOSYN with vancomycin may increase the incidence of acute kidney injury. Monitor kidney function in patients receiving ZOSYN and vancomycin. (7.3)
- Monitor coagulation parameters in patients receiving ZOSYN and heparin or oral anticoagulants. (7.4)
- ZOSYN may prolong the neuromuscular blockade of vecuronium and other non-depolarizing muscle relaxants. Monitor for adverse reactions related to neuromuscular blockade (7.5)

### USE IN SPECIFIC POPULATIONS

Dosage in patients with renal impairment (≤40 mL/min of CRCL) should be reduced to the degree of actual renal function impairment. (2.3, 8.6)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 11/2018
5.8 Development of Drug-Resistant Bacteria

6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Post-Marketing Experience
6.3 Additional Experience with piperacillin

7 DRUG INTERACTIONS
7.1 Aminoglycosides
7.2 Probenecid
7.3 Vancomycin
7.4 Anticoagulants
7.5 Vecuronium
7.6 Methotrexate
7.7 Effects on Laboratory Tests

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Renal Impairment
8.7 Hepatic Impairment
8.8 Patients with Cystic Fibrosis

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
12.4 Microbiology

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

To reduce the development of drug-resistant bacteria and maintain the effectiveness of ZOSYN and other antibacterial drugs, ZOSYN should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

1 INDICATIONS AND USAGE

ZOSYN is a combination product consisting of a penicillin-class antibacterial, piperacillin, and a β-lactamase inhibitor, tazobactam, indicated for the treatment of patients with moderate to severe infections caused by susceptible isolates of the designated bacteria in the conditions listed below.

1.1 Intra-abdominal Infections

Appendicitis (complicated by rupture or abscess) and peritonitis caused by β-lactamase producing isolates of Escherichia coli or the following members of the Bacteroides fragilis group: B. fragilis, B.
ovatus, B. thetaiotaomicron, or B. vulgatus. The individual members of this group were studied in fewer than 10 cases.

1.2 Skin and Skin Structure Infections
Uncomplicated and complicated skin and skin structure infections, including cellulitis, cutaneous abscesses and ischemic/diabetic foot infections caused by β-lactamase producing isolates of Staphylococcus aureus.

1.3 Female Pelvic Infections
Postpartum endometritis or pelvic inflammatory disease caused by β-lactamase producing isolates of Escherichia coli.

1.4 Community-acquired Pneumonia
Community-acquired pneumonia (moderate severity only) caused by β-lactamase producing isolates of Haemophilus influenzae.

1.5 Nosocomial Pneumonia
Nosocomial pneumonia (moderate to severe) caused by β-lactamase producing isolates of Staphylococcus aureus and by piperacillin/tazobactam-susceptible Acinetobacter baumannii, Haemophilus influenzae, Klebsiella pneumoniae, and Pseudomonas aeruginosa (Nosocomial pneumonia caused by P. aeruginosa should be treated in combination with an aminoglycoside) [see Dosage and Administration (2)].

1.6 Usage
To reduce the development of drug-resistant bacteria and maintain the effectiveness of ZOSYN and other antibacterial drugs, ZOSYN should be used only to treat or prevent infections that are proven or strongly suspected to be caused by 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.

2 DOSAGE AND ADMINISTRATION
ZOSYN should be administered by intravenous infusion over 30 minutes.

2.1 Adult Patients
The usual total daily dose of ZOSYN for adults is 3.375 g every six hours totaling 13.5 g (12.0 g piperacillin/1.5 g tazobactam). The usual duration of ZOSYN treatment is from 7 to 10 days.

ZOSYN should be administered by intravenous infusion over 30 minutes.

2.2 Nosocomial Pneumonia
Initial presumptive treatment of patients with nosocomial pneumonia should start with ZOSYN at a dosage of 4.5 g every six hours plus an aminoglycoside, totaling 18.0 g (16.0 g piperacillin/2.0 g tazobactam). The recommended duration of ZOSYN treatment for nosocomial pneumonia is 7 to 14 days. Treatment with the aminoglycoside should be continued in patients from whom P. aeruginosa is isolated.

2.3 Renal Impairment
In patients with renal impairment (creatinine clearance ≤ 40 mL/min) and dialysis patients (hemodialysis and CAPD), the intravenous dose of ZOSYN should be reduced to the degree of actual renal function impairment. The recommended daily doses of ZOSYN for patients with renal impairment are as follows:
Table 1: Recommended Dosing of ZOSYN in Patients with Normal Renal Function and Renal-Impairment (As total grams piperacillin/tazobactam)

<table>
<thead>
<tr>
<th>Renal Function (creatinine clearance, mL/min)</th>
<th>All Indications (except nosocomial pneumonia)</th>
<th>Nosocomial Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;40 mL/min</td>
<td>3.375 q 6 h</td>
<td>4.5 q 6 h</td>
</tr>
<tr>
<td>20–40 mL/min*</td>
<td>2.25 q 6 h</td>
<td>3.375 q 6 h</td>
</tr>
<tr>
<td>&lt;20 mL/min*</td>
<td>2.25 q 8 h</td>
<td>2.25 q 6 h</td>
</tr>
<tr>
<td>Hemodialysis†</td>
<td>2.25 q 12 h</td>
<td>2.25 q 8 h</td>
</tr>
<tr>
<td>CAPD</td>
<td>2.25 q 12 h</td>
<td>2.25 q 8 h</td>
</tr>
</tbody>
</table>

* Creatinine clearance for patients not receiving hemodialysis
† 0.75 g (0.67 g piperacillin/0.08 g tazobactam) should be administered following each hemodialysis session on hemodialysis days

For patients on hemodialysis, the maximum dose is 2.25 g every twelve hours for all indications other than nosocomial pneumonia and 2.25 g every eight hours for nosocomial pneumonia. Since hemodialysis removes 30% to 40% of the administered dose, an additional dose of 0.75 g ZOSYN (0.67 g piperacillin/0.08 g tazobactam) should be administered following each dialysis period on hemodialysis days. No additional dosage of ZOSYN is necessary for CAPD patients.

2.4 Pediatric Patients

For children with appendicitis and/or peritonitis 9 months of age or older, weighing up to 40 kg, and with normal renal function, the recommended ZOSYN dosage is 100 mg piperacillin/12.5 mg tazobactam per kilogram of body weight, every 8 hours. For pediatric patients between 2 months and 9 months of age, the recommended ZOSYN dosage based on pharmacokinetic modeling, is 80 mg piperacillin/10 mg tazobactam per kilogram of body weight, every 8 hours [see Use in Specific Populations (8.4) and Clinical Pharmacology (12.3)]. Pediatric patients weighing over 40 kg and with normal renal function should receive the adult dose.

It has not been determined how to adjust ZOSYN dosage in pediatric patients with renal impairment.

2.5 Reconstitution and Dilution of Powder Formulations

Pharmacy bulk vials

Reconstituted stock solution must be transferred and further diluted for intravenous infusion.

The pharmacy bulk vial is for use in a hospital pharmacy admixture service only under a laminar flow hood. After reconstitution, entry into the vial must be made with a sterile transfer set or other sterile dispensing device, and contents should be dispensed as aliquots into intravenous solution using aseptic technique. Use entire contents of pharmacy bulk vial promptly. Discard unused portion after 24 hours if stored at room temperature (20°C to 25°C [68°F to 77°F]), or after 48 hours if stored at refrigerated temperature (2°C to 8°C [36°F to 46°F]).

Reconstitute the pharmacy bulk vial with exactly 152 mL of a compatible reconstitution diluent, listed below, to a concentration of 200 mg/mL of piperacillin and 25 mg/mL of tazobactam. Shake well until dissolved. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to and during administration whenever solution and container permit.

Single dose vials

Reconstitute ZOSYN vials with a compatible reconstitution diluent from the list provided below. 2.25 g, 3.375 g, and 4.5 g ZOSYN should be reconstituted with 10 mL, 15 mL, and 20 mL, respectively. Swirl until dissolved.
Compatible Reconstitution Diluents for Pharmacy and Single Dose Vials

- 0.9% sodium chloride for injection
- Sterile water for injection
- Dextrose 5%
- Bacteriostatic saline/parabens
- Bacteriostatic water/parabens
- Bacteriostatic saline/benzyl alcohol
- Bacteriostatic water/benzyl alcohol

Reconstituted ZOSYN solutions for both bulk and single dose vials should be further diluted (recommended volume per dose of 50 mL to 150 mL) in a compatible intravenous solution listed below. Administer by infusion over a period of at least 30 minutes. During the infusion it is desirable to discontinue the primary infusion solution.

Compatible Intravenous Solutions for Pharmacy and Single Dose Vials

- 0.9% sodium chloride for injection
- Sterile water for injection
- Dextran 6% in saline
- Dextrose 5%
- Lactated Ringer's Solution (compatible only with reformulated ZOSYN containing EDTA and is compatible for co-administration via a Y-site)

ZOSYN should not be mixed with other drugs in a syringe or infusion bottle since compatibility has not been established.

ZOSYN is not chemically stable in solutions that contain only sodium bicarbonate and solutions that significantly alter the pH.

ZOSYN should not be added to blood products or albumin hydrolysates. Parenteral drug products should be inspected visually for particulate matter or discoloration prior to administration, whenever solution and container permit.

Stability of ZOSYN Powder Formulations Following Reconstitution

ZOSYN reconstituted from bulk and single vials is stable in glass and plastic containers (plastic syringes, I.V. bags and tubing) when used with compatible diluents. The pharmacy bulk vial should NOT be frozen after reconstitution. Discard unused portions after storage for 24 hours at room temperature or after storage for 48 hours at refrigerated temperature (2°C to 8°C [36°F to 46°F]).

Single dose or pharmacy vials should be used immediately after reconstitution. Discard any unused portion after 24 hours if stored at room temperature (20°C to 25°C [68°F to 77°F]), or after 48 hours if stored at refrigerated temperature (2°C to 8°C [36°F to 46°F]). Vials should not be frozen after reconstitution.

Stability studies in the I.V. bags have demonstrated chemical stability (potency, pH of reconstituted solution and clarity of solution) for up to 24 hours at room temperature and up to one week at refrigerated temperature. ZOSYN contains no preservatives. Appropriate consideration of aseptic technique should be used.

ZOSYN reconstituted from bulk and single vials can be used in ambulatory intravenous infusion pumps. Stability of ZOSYN in an ambulatory intravenous infusion pump has been demonstrated for a period of 12 hours at room temperature. Each dose was reconstituted and diluted to a volume of 37.5 mL or 25 mL. One-day supplies of dosing solution were aseptically transferred into the medication reservoir (I.V. bags or cartridge). The reservoir was fitted to a preprogrammed ambulatory intravenous infusion pump per the manufacturer's instructions. Stability of ZOSYN is not affected when administered using an

1 Maximum recommended volume per dose of sterile water for injection is 50 mL.
ambulatory intravenous infusion pump.

2.6 Directions for Use of ZOSYN in GALAXY Containers

ZOSYN Injection is to be administered using sterile equipment, after thawing to room temperature.

ZOSYN containing EDTA is compatible for co-administration via a Y-site intravenous tube with Lactated Ringer's injection, USP.

Do not add supplementary medication.

Unused portions of ZOSYN should be discarded.

CAUTION: Do not use plastic containers in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is complete.

Thawing of Plastic Container

Thaw frozen container at room temperature 20°C to 25°C [68°F to 77°F] or under refrigeration (2°C to 8°C [36°F to 46°F]). Do not force thaw by immersion in water baths or by microwave irradiation.

Check for minute leaks by squeezing container firmly. If leaks are detected, discard solution as sterility may be impaired.

The container should be visually inspected. Components of the solution may precipitate in the frozen state and will dissolve upon reaching room temperature with little or no agitation. Potency is not affected. Agitate after solution has reached room temperature. If after visual inspection, the solution remains cloudy or if an insoluble precipitate is noted or if any seals or outlet ports are not intact, the container should be discarded.

Administer by infusion over a period of at least 30 minutes. During the infusion it is desirable to discontinue the primary infusion solution.

Storage

Store in a freezer capable of maintaining a temperature of -20°C (-4°F).

For GALAXY containers, the thawed solution is stable for 14 days under refrigeration (2°C to 8°C [36°F to 46°F]) or 24 hours at room temperature 20°C to 25°C [68°F to 77°F]. Do not refreeze thawed ZOSYN.

2.7 Compatibility with Aminoglycosides

Due to the in vitro inactivation of aminoglycosides by piperacillin, ZOSYN and aminoglycosides are recommended for separate administration. ZOSYN and aminoglycosides should be reconstituted, diluted, and administered separately when concomitant therapy with aminoglycosides is indicated [see Drug Interactions (7.1)].

In circumstances where co-administration via Y-site is necessary, ZOSYN formulations containing EDTA are compatible for simultaneous co-administration via Y-site infusion only with the following aminoglycosides under the following conditions:

<table>
<thead>
<tr>
<th>Aminoglycoside</th>
<th>ZOSYN Dose (grams)</th>
<th>ZOSYN Diluent Volume * (mL)</th>
<th>Aminoglycoside Concentration Range † (mg/mL)</th>
<th>Acceptable Diluents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>2.25</td>
<td>50</td>
<td>1.75 – 7.5</td>
<td>0.9% sodium chloride or 5% dextrose</td>
</tr>
<tr>
<td></td>
<td>3.375</td>
<td>100</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.5</td>
<td>150</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Gentamicin

<table>
<thead>
<tr>
<th>Concentration</th>
<th>2.25</th>
<th>3.375</th>
<th>4.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diluent</td>
<td>50</td>
<td>100</td>
<td>150</td>
</tr>
<tr>
<td>Concentration</td>
<td>0.7 – 3.32</td>
<td>0.9% sodium chloride or 5% dextrose</td>
<td></td>
</tr>
</tbody>
</table>

* Diluent volumes apply only to single vials and bulk pharmacy containers

† The concentration ranges in Table 2 are based on administration of the aminoglycoside in divided doses (10–15 mg/kg/day in two daily doses for amikacin and 3–5 mg/kg/day in three daily doses for gentamicin). Administration of amikacin or gentamicin in a single daily dose or in doses exceeding those stated above via Y-site with ZOSYN containing EDTA has not been evaluated. See package insert for each aminoglycoside for complete Dosage and Administration instructions.

‡ ZOSYN 3.375 g per 50 mL GALAXY containers are NOT compatible with gentamicin for co-administration via a Y-site due to the higher concentrations of piperacillin and tazobactam.

Only the concentration and diluents for amikacin or gentamicin with the dosages of ZOSYN listed above have been established as compatible for co-administration via Y-site infusion. Simultaneous co-administration via Y-site infusion in any manner other than listed above may result in inactivation of the aminoglycoside by ZOSYN.

ZOSYN is not compatible with tobramycin for simultaneous co-administration via Y-site infusion. Compatibility of ZOSYN with other aminoglycosides has not been established.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

3 DOSAGE FORMS AND STRENGTHS

ZOSYN® (piperacillin and tazobactam) for Injection is supplied as a white to off-white powder in vials of the following sizes:

Each ZOSYN 2.25 g vial provides piperacillin sodium equivalent to 2 grams of piperacillin and tazobactam sodium equivalent to 0.25 g of tazobactam.

Each ZOSYN 3.375 g vial provides piperacillin sodium equivalent to 3 grams of piperacillin and tazobactam sodium equivalent to 0.375 g of tazobactam.

Each ZOSYN 4.5 g vial provides piperacillin sodium equivalent to 4 grams of piperacillin and tazobactam sodium equivalent to 0.5 g of tazobactam.

Each ZOSYN 40.5 g pharmacy bulk vial contains piperacillin sodium equivalent to 36 grams of piperacillin and tazobactam sodium equivalent to 4.5 grams tazobactam.

ZOSYN® (piperacillin and tazobactam) Injection is supplied in GALAXY Containers as a frozen, isosmotic, sterile, non-pyrogenic solution in single-dose plastic containers:

2.25 g (piperacillin sodium equivalent to 2 g piperacillin/tazobactam sodium equivalent to 0.25 g tazobactam) in 50 mL.

3.375 g (piperacillin sodium equivalent to 3 g piperacillin/tazobactam sodium equivalent to 0.375 g tazobactam) in 50 mL.

4.5 g (piperacillin sodium equivalent to 4 g piperacillin/tazobactam sodium equivalent to 0.5 g tazobactam) in 100 mL.

4 CONTRAINDICATIONS

ZOSYN is contraindicated in patients with a history of allergic reactions to any of the penicillins, cephalosporins, or β-lactamase inhibitors.
5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Adverse Reactions
Serious and occasionally fatal hypersensitivity (anaphylactic/anaphylactoid) reactions (including shock) have been reported in patients receiving therapy with ZOSYN. These reactions are more likely to occur in individuals with a history of penicillin, cephalosporin, or carbapenem hypersensitivity or a history of sensitivity to multiple allergens. Before initiating therapy with ZOSYN, careful inquiry should be made concerning previous hypersensitivity reactions. If an allergic reaction occurs, ZOSYN should be discontinued and appropriate therapy instituted.

5.2 Severe Cutaneous Adverse Reactions
ZOSYN may cause severe cutaneous adverse reactions, such as Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, and acute generalized exanthematous pustulosis. If patients develop a skin rash they should be monitored closely and ZOSYN discontinued if lesions progress.

5.3 Hematologic Adverse Reactions
Bleeding manifestations have occurred in some patients receiving β-lactam drugs, including piperacillin. These reactions have sometimes been associated with abnormalities of coagulation tests such as clotting time, platelet aggregation and prothrombin time, and are more likely to occur in patients with renal failure. If bleeding manifestations occur, ZOSYN should be discontinued and appropriate therapy instituted.

The leukopenia/neutropenia associated with ZOSYN administration appears to be reversible and most frequently associated with prolonged administration.

Periodic assessment of hematopoietic function should be performed, especially with prolonged therapy, i.e., ≥ 21 days [see Adverse Reactions (6.1)].

5.4 Central Nervous System Adverse Reactions
As with other penicillins, patients may experience neuromuscular excitability or convulsions if higher than recommended doses are given intravenously (particularly in the presence of renal failure).

5.5 Nephrotoxicity in Critically Ill Patients
The use of ZOSYN was found to be an independent risk factor for renal failure and was associated with delayed recovery of renal function as compared to other beta-lactam antibacterial drugs in a randomized, multicenter, controlled trial in critically ill patients [see Adverse Reactions (6.1)]. Based on this study, alternative treatment options should be considered in the critically ill population. If alternative treatment options are inadequate or unavailable, monitor renal function during treatment with ZOSYN [see Dosage and Administration (2.3)].

Combined use of piperacillin/tazobactam and vancomycin may be associated with an increased incidence of acute kidney injury [see Drug Interactions (7.3)].

5.6 Electrolyte Effects
ZOSYN contains a total of 2.84 mEq (65 mg) of Na\(^+\) (sodium) per gram of piperacillin in the combination product. This should be considered when treating patients requiring restricted salt intake. Periodic electrolyte determinations should be performed in patients with low potassium reserves, and the possibility of hypokalemia should be kept in mind with patients who have potentially low potassium reserves and who are receiving cytotoxic therapy or diuretics.

5.7 Clostridium difficile Associated Diarrhea
Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial
agents, including ZOSYN, 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.

### 5.8 Development of Drug-Resistant Bacteria

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

### 6 ADVERSE REACTIONS

#### 6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

During the initial clinical investigations, 2621 patients worldwide were treated with ZOSYN in phase 3 trials. In the key North American monotherapy clinical trials (n=830 patients), 90% of the adverse events reported were mild to moderate in severity and transient in nature. However, in 3.2% of the patients treated worldwide, ZOSYN was discontinued because of adverse events primarily involving the skin (1.3%), including rash and pruritus; the gastrointestinal system (0.9%), including diarrhea, nausea, and vomiting; and allergic reactions (0.5%).

#### Table 3: Adverse Reactions from ZOSYN Monotherapy Clinical Trials

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Adverse Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal disorders</td>
<td>Diarrhea (11.3%)</td>
</tr>
<tr>
<td></td>
<td>Constipation (7.7%)</td>
</tr>
<tr>
<td></td>
<td>Nausea (6.9%)</td>
</tr>
<tr>
<td></td>
<td>Vomiting (3.3%)</td>
</tr>
<tr>
<td></td>
<td>Dyspepsia (3.3%)</td>
</tr>
<tr>
<td></td>
<td>Abdominal pain (1.3%)</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Fever (2.4%)</td>
</tr>
<tr>
<td></td>
<td>Injection site reaction (≤1%)</td>
</tr>
<tr>
<td></td>
<td>Rigors (≤1%)</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Anaphylaxis (≤1%)</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td>Candidiasis (1.6%)</td>
</tr>
<tr>
<td></td>
<td>Pseudomembranous colitis (≤1%)</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td></td>
</tr>
</tbody>
</table>
Hypoglycemia (≤1%)

**Musculoskeletal and connective tissue disorders**
- Myalgia (≤1%)
- Arthralgia (≤1%)

**Nervous system disorders**
- Headache (7.7%)

**Psychiatric disorders**
- Insomnia (6.6%)

**Skin and subcutaneous tissue disorders**
- Rash (4.2%, including maculopapular, bullous, and urticarial)
- Pruritus (3.1%)
- Purpura (≤1%)

**Vascular disorders**
- Phlebitis (1.3%)
- Thrombophlebitis (≤1%)
- Hypotension (≤1%)
- Flushing (≤1%)

**Respiratory, thoracic and mediastinal disorders**
- Epistaxis (≤1%)

### Nosocomial Pneumonia Trials

Two trials of nosocomial lower respiratory tract infections were conducted. In one study, 222 patients were treated with ZOSYN in a dosing regimen of 4.5 g every 6 hours in combination with an aminoglycoside and 215 patients were treated with imipenem/cilastatin (500 mg/500 mg q6h) in combination with an aminoglycoside. In this trial, treatment-emergent adverse events were reported by 402 patients, 204 (91.9%) in the piperacillin/tazobactam group and 198 (92.1%) in the imipenem/cilastatin group. Twenty-five (11.0%) patients in the piperacillin/tazobactam group and 14 (6.5%) in the imipenem/cilastatin group (p > 0.05) discontinued treatment due to an adverse event.

The second trial used a dosing regimen of 3.375 g given every 4 hours with an aminoglycoside.

### Table 4: Adverse Reactions from ZOSYN Plus Aminoglycoside Clinical Trials*

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Adverse Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood and lymphatic system disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Thrombocytemia (1.4%)</td>
<td></td>
</tr>
<tr>
<td>Anemia (≤1%)</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia (≤1%)</td>
<td></td>
</tr>
<tr>
<td>Eosinophilia (≤1%)</td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal disorders</strong></td>
<td></td>
</tr>
<tr>
<td>Diarrhea (20%)</td>
<td></td>
</tr>
<tr>
<td>Constipation (8.4%)</td>
<td></td>
</tr>
<tr>
<td>Nausea (5.8%)</td>
<td></td>
</tr>
<tr>
<td>Vomiting (2.7%)</td>
<td></td>
</tr>
<tr>
<td>Dyspepsia (1.9%)</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain (1.8%)</td>
<td></td>
</tr>
<tr>
<td>Stomatitis (≤1%)</td>
<td></td>
</tr>
</tbody>
</table>
General disorders and administration site conditions

- Fever (3.2%)
- Injection site reaction (≤1%)

Infections and infestations

- Oral candidiasis (3.9%)
- Candidiasis (1.8%)

Investigations

- BUN increased (1.8%)
- Blood creatinine increased (1.8%)
- Liver function test abnormal (1.4%)
- Alkaline phosphatase increased (≤1%)
- Aspartate aminotransferase increased (≤1%)
- Alanine aminotransferase increased (≤1%)

Metabolism and nutrition disorders

- Hypoglycemia (≤1%)
- Hypokalemia (≤1%)

Nervous system disorders

- Headache (4.5%)

Psychiatric disorders

- Insomnia (4.5%)

Renal and urinary disorders

- Renal failure (≤1%)

Skin and subcutaneous tissue disorders

- Rash (3.9%)
- Pruritus (3.2%)

Vascular disorders

- Thrombophlebitis (1.3%)
- Hypotension (1.3%)

* For adverse drug reactions that appeared in both studies the higher frequency is presented.

Other trials: Nephrotoxicity

In a randomized, multicenter, controlled trial in 1200 adult critically ill patients, piperacillin/tazobactam was found to be a risk factor for renal failure (odds ratio 1.7, 95% CI 1.18 to 2.43), and associated with delayed recovery of renal function as compared to other beta-lactam antibacterial drugs. [see Warnings and Precautions (5.5)].

Pediatrics

Studies of ZOSYN in pediatric patients suggest a similar safety profile to that seen in adults. In a prospective, randomized, comparative, open-label clinical trial of pediatric patients with severe intra-abdominal infections (including appendicitis and/or peritonitis), 273 patients were treated with ZOSYN (112.5 mg/kg every 8 hours) and 269 patients were treated with cefotaxime (50 mg/kg) plus metronidazole (7.5 mg/kg) every 8 hours. In this trial, treatment-emergent adverse events were reported by 146 patients, 73 (26.7%) in the ZOSYN group and 73 (27.1%) in the cefotaxime/metronidazole group. Six patients (2.2%) in the ZOSYN group and 5 patients (1.9%) in the cefotaxime/metronidazole group discontinued due to an adverse event.

Adverse Laboratory Events (Seen During Clinical Trials)

Of the trials reported, including that of nosocomial lower respiratory tract infections in which a higher
dose of ZOSYN was used in combination with an aminoglycoside, changes in laboratory parameters include:

**Hematologic**—decreases in hemoglobin and hematocrit, thrombocytopenia, increases in platelet count, eosinophilia, leukopenia, neutropenia. These patients were withdrawn from therapy; some had accompanying systemic symptoms (e.g., fever, rigors, chills)

**Coagulation**—positive direct Coombs’ test, prolonged prothrombin time, prolonged partial thromboplastin time

**Hepatic**—transient elevations of AST (SGOT), ALT (SGPT), alkaline phosphatase, bilirubin

**Renal**—increases in serum creatinine, blood urea nitrogen

Additional laboratory events include abnormalities in electrolytes (i.e., increases and decreases in sodium, potassium, and calcium), hyperglycemia, decreases in total protein or albumin, blood glucose decreased, gamma-glutamyltransferase increased, hypokalemia, and bleeding time prolonged.

### 6.2 Post-Marketing Experience

In addition to the adverse drug reactions identified in clinical trials in Table 3 and Table 4, the following adverse reactions have been identified during post-approval use of ZOSYN. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

**Hepatobiliary**—hepatitis, jaundice

**Hematologic**—hemolytic anemia, agranulocytosis, pancytopenia

**Immune**—hypersensitivity reactions, anaphylactic/anaphylactoid reactions (including shock)

**Renal**—interstitial nephritis

**Psychiatric disorders**—delirium

**Respiratory**—eosinophilic pneumonia

**Skin and Appendages**—erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, (DRESS), acute generalized exanthematous pustulosis (AGEP), dermatitis exfoliative

### 6.3 Additional Experience with piperacillin

The following adverse reaction has also been reported for piperacillin for injection:

**Skeletal**—prolonged muscle relaxation [see Drug Interactions (7.5)].

Post-marketing experience with ZOSYN in pediatric patients suggests a similar safety profile to that seen in adults.

### 7 DRUG INTERACTIONS

#### 7.1 Aminoglycosides

Piperacillin may inactivate aminoglycosides by converting them to microbiologically inert amides.

*In vivo* inactivation:

When aminoglycosides are administered in conjunction with piperacillin to patients with end-stage renal disease requiring hemodialysis, the concentrations of the aminoglycosides (especially tobramycin) may be significantly reduced and should be monitored.

Sequential administration of ZOSYN and tobramycin to patients with either normal renal function or mild to moderate renal impairment has been shown to modestly decrease serum concentrations of tobramycin.
but no dosage adjustment is considered necessary.

In vitro inactivation:

Due to the in vitro inactivation of aminoglycosides by piperacillin, ZOSYN and aminoglycosides are recommended for separate administration. ZOSYN and aminoglycosides should be reconstituted, diluted, and administered separately when concomitant therapy with aminoglycosides is indicated. ZOSYN, which contains EDTA, is compatible with amikacin and gentamicin for simultaneous Y-site infusion in certain diluents and at specific concentrations. ZOSYN is not compatible with tobramycin for simultaneous Y-site infusion [see Dosage and Administration (2.7)].

7.2 Probenecid

Probenecid administered concomitantly with ZOSYN prolongs the half-life of piperacillin by 21% and that of tazobactam by 71% because probenecid inhibits tubular renal secretion of both piperacillin and tazobactam. Probenecid should not be co-administered with ZOSYN unless the benefit outweighs the risk.

7.3 Vancomycin

Studies have detected an increased incidence of acute kidney injury in patients concomitantly administered piperacillin/tazobactam and vancomycin as compared to vancomycin alone [see Warnings and Precautions (5.5)]. Monitor kidney function in patients concomitantly administered with piperacillin/tazobactam and vancomycin.

No pharmacokinetic interactions have been noted between piperacillin/tazobactam and vancomycin.

7.4 Anticoagulants

Coagulation parameters should be tested more frequently and monitored regularly during simultaneous administration of high doses of heparin, oral anticoagulants, or other drugs that may affect the blood coagulation system or the thrombocyte function [see Warnings and Precautions (5.3)].

7.5 Vecuronium

Piperacillin when used concomitantly with vecuronium has been implicated in the prolongation of the neuromuscular blockade of vecuronium. ZOSYN could produce the same phenomenon if given along with vecuronium. Due to their similar mechanism of action, it is expected that the neuromuscular blockade produced by any of the non-depolarizing muscle relaxants could be prolonged in the presence of piperacillin. Monitor for adverse reactions related to neuromuscular blockade (See package insert for vecuronium bromide).

7.6 Methotrexate

Limited data suggests that co-administration of methotrexate and piperacillin may reduce the clearance of methotrexate due to competition for renal secretion. The impact of tazobactam on the elimination of methotrexate has not been evaluated. If concurrent therapy is necessary, serum concentrations of methotrexate as well as the signs and symptoms of methotrexate toxicity should be frequently monitored.

7.7 Effects on Laboratory Tests

There have been reports of positive test results using the Bio-Rad Laboratories Platelia Aspergillus EIA test in patients receiving piperacillin/tazobactam injection who were subsequently found to be free of Aspergillus infection. Cross-reactions with non-Aspergillus polysaccharides and polyfuranoses with the Bio-Rad Laboratories Platelia Aspergillus EIA test have been reported. Therefore, positive test results in patients receiving piperacillin/tazobactam should be interpreted cautiously and confirmed
by other diagnostic methods.

As with other penicillins, the administration of ZOSYN may result in a false-positive reaction for glucose in the urine using a copper-reduction method (CLINITEST®). It is recommended that glucose tests based on enzymatic glucose oxidase reactions be used.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Piperacillin and tazobactam cross the placenta in humans. However, there are insufficient data with piperacillin and/or tazobactam in pregnant women to inform a drug-associated risk for major birth defects and miscarriage. No fetal structural abnormalities were observed in rats or mice when piperacillin/tazobactam was administered intravenously during organogenesis at doses 1 to 2 times and 2 to 3 times the human dose of piperacillin and tazobactam, respectively, based on body-surface area (mg/m²). However, fetotoxicity in the presence of maternal toxicity was observed in developmental toxicity and peri/postnatal studies conducted in rats (intraperitoneal administration prior to mating and throughout gestation or from gestation day 17 through lactation day 21) at doses less than the maximum recommended human daily dose based on body-surface area (mg/m²) [see Data].

The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2–4% and 15–20%, respectively.

Data

Animal Data

In embryo-fetal development studies in mice and rats, pregnant animals received intravenous doses of piperacillin/tazobactam up to 3000/750 mg/kg/day during the period of organogenesis. There was no evidence of teratogenicity up to the highest dose evaluated, which is 1 to 2 times and 2 to 3 times the human dose of piperacillin and tazobactam, in mice and rats respectively, based on body-surface area (mg/m²). Fetal body weights were reduced in rats at maternally toxic doses at or above 500/62.5 mg/kg/day, minimally representing 0.4 times the human dose of both piperacillin and tazobactam based on body-surface area (mg/m²).

A fertility and general reproduction study in rats using intraperitoneal administration of tazobactam or the combination piperacillin/tazobactam prior to mating and through the end of gestation, reported a decrease in litter size in the presence of maternal toxicity at 640 mg/kg/day tazobactam (4 times the human dose of tazobactam based on body-surface area), and decreased litter size and an increase in fetuses with ossification delays and variations of ribs, concurrent with maternal toxicity at ≥640/160 mg/kg/day piperacillin/tazobactam (0.5 times and 1 times the human dose of piperacillin and tazobactam, respectively, based on body-surface area).

Peri/postnatal development in rats was impaired with reduced pup weights, increased stillbirths, and increased pup mortality concurrent with maternal toxicity after intraperitoneal administration of tazobactam alone at doses ≥320 mg/kg/day (2 times the human dose based on body surface area) or of the combination piperacillin/tazobactam at doses ≥640/160 mg/kg/day (0.5 times and 1 times the human dose of piperacillin and tazobactam, respectively, based on body-surface area) from gestation day 17 through lactation day 21.

8.2 Lactation

Risk Summary

Piperacillin is excreted in human milk; tazobactam concentrations in human milk have not been studied. No information is available on the effects of piperacillin and tazobactam on the breast-fed child or on
milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for ZOSYN and any potential adverse effects on the breastfed child from ZOSYN or from the underlying maternal condition.

8.4 Pediatric Use
Use of ZOSYN in pediatric patients 2 months of age or older with appendicitis and/or peritonitis is supported by evidence from well-controlled studies and pharmacokinetic studies in adults and in pediatric patients. This includes a prospective, randomized, comparative, open-label clinical trial with 542 pediatric patients 2–12 years of age with complicated intra-abdominal infections, in which 273 pediatric patients received piperacillin/tazobactam. Safety and efficacy in pediatric patients less than 2 months of age have not been established [see Clinical Pharmacology (12) and Dosage and Administration (2)].

It has not been determined how to adjust ZOSYN dosage in pediatric patients with renal impairment.

8.5 Geriatric Use
Patients over 65 years are not at an increased risk of developing adverse effects solely because of age. However, dosage should be adjusted in the presence of renal impairment [see Dosage and Administration (2)].

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

ZOSYN contains 65 mg (2.84 mEq) of sodium per gram of piperacillin in the combination product. At the usual recommended doses, patients would receive between 780 and 1040 mg/day (34.1 and 45.5 mEq) of sodium. The geriatric population may respond with a blunted natriuresis to salt loading. This may be clinically important with regard to such diseases as congestive heart failure.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

8.6 Renal Impairment
In patients with creatinine clearance ≤ 40 mL/min and dialysis patients (hemodialysis and CAPD), the intravenous dose of ZOSYN should be reduced to the degree of renal function impairment [see Dosage and Administration (2)].

8.7 Hepatic Impairment
Dosage adjustment of ZOSYN is not warranted in patients with hepatic cirrhosis [see Clinical Pharmacology (12.3)].

8.8 Patients with Cystic Fibrosis
As with other semisynthetic penicillins, piperacillin therapy has been associated with an increased incidence of fever and rash in cystic fibrosis patients.

10 OVERDOSAGE
There have been postmarketing reports of overdose with piperacillin/tazobactam. The majority of those events experienced, including nausea, vomiting, and diarrhea, have also been reported with the usual recommended dosages. Patients may experience neuromuscular excitability or convulsions if higher than recommended doses are given intravenously (particularly in the presence of renal failure) [see Warnings and Precautions (5.4)].
Treatment should be supportive and symptomatic according to the patient's clinical presentation. Excessive serum concentrations of either piperacillin or tazobactam may be reduced by hemodialysis. Following a single 3.375 g dose of piperacillin/tazobactam, the percentage of the piperacillin and tazobactam dose removed by hemodialysis was approximately 31% and 39%, respectively [see Clinical Pharmacology (12)].

**11 DESCRIPTION**

ZOSYN (piperacillin and tazobactam) for Injection and ZOSYN (piperacillin and tazobactam) Injection are injectable antibacterial combination products consisting of the semisynthetic antibacterial piperacillin sodium and the β-lactamase inhibitor tazobactam sodium for intravenous administration.

Piperacillin sodium is derived from D(-)-α-aminobenzyl-penicillin. The chemical name of piperacillin sodium is sodium (2S,5R,6R)-6-[(R)-2-(4-ethyl-2,3-dioxo-1-piperazine-carboxamido)-2-phenylacetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate. The chemical formula is C_{23}H_{26}N_{5}NaO_{7}S and the molecular weight is 539.5. The chemical structure of piperacillin sodium is:

![Chemical structure of piperacillin sodium](image)

Tazobactam sodium, a derivative of the penicillin nucleus, is a penicillanic acid sulfone. Its chemical name is sodium (2S,3S,5R)-3-methyl-7-oxo-3-(1H-1,2,3-triazol-1-ylmethyl)-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylate-4,4-dioxide. The chemical formula is C_{10}H_{11}N_{4}NaO_{5}S and the molecular weight is 322.3. The chemical structure of tazobactam sodium is:

![Chemical structure of tazobactam sodium](image)

ZOSYN (piperacillin and tazobactam) for Injection, is a white to off-white sterile, cryodesiccated powder consisting of piperacillin and tazobactam as their sodium salts packaged in glass vials. The formulation also contains edetate disodium dihydrate (EDTA) and sodium citrate.

Each ZOSYN 2.25 g single dose vial contains an amount of drug sufficient for withdrawal of piperacillin sodium equivalent to 2 grams of piperacillin and tazobactam sodium equivalent to 0.25 g of tazobactam. The product also contains 0.5 mg of EDTA per vial.

Each ZOSYN 3.375 g single dose vial contains an amount of drug sufficient for withdrawal of
piperacillin sodium equivalent to 3 grams of piperacillin and tazobactam sodium equivalent to 0.375 g of
tazobactam. The product also contains 0.75 mg of EDTA per vial.

Each ZOSYN 4.5 g single dose vial contains an amount of drug sufficient for withdrawal of piperacillin
sodium equivalent to 4 grams of piperacillin and tazobactam sodium equivalent to 0.5 g of tazobactam.
The product also contains 1 mg of EDTA per vial.

Each Zosyn 40.5 g pharmacy bulk vial contains piperacillin sodium equivalent to 36 grams of
piperacillin and tazobactam sodium equivalent to 4.5 g of tazobactam sufficient for delivery of multiple
doses.

ZOSYN Injection in the GALAXY Container is a frozen iso-osmotic sterile non-pyrogenic premixed
solution. The components and dosage formulations are given in the table below:

Table 5: ZOSYN In GALAXY Containers Premixed Frozen Solution

<table>
<thead>
<tr>
<th>Component</th>
<th>Function</th>
<th>Dosage Formulations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piperacillin</td>
<td>active ingredient</td>
<td>2 g, 3 g, 4 g</td>
</tr>
<tr>
<td>Tazobactam</td>
<td>β-lactamase inhibitor</td>
<td>250 mg, 375 mg, 500 mg</td>
</tr>
<tr>
<td>Dextrose Hydrous</td>
<td>osmolality adjusting agent</td>
<td>1 g, 350 mg, 2 g</td>
</tr>
<tr>
<td>Sodium Citrate Dihydrate</td>
<td>buffering agent</td>
<td>100 mg, 150 mg, 200 mg</td>
</tr>
<tr>
<td>Edetate Disodium Dihydrate</td>
<td>metal chelator</td>
<td>0.5 mg, 0.75 mg, 1 mg</td>
</tr>
<tr>
<td>Water for Injection</td>
<td>solvent</td>
<td>q.s. 50 mL, q.s. 50 mL, q.s. 100 mL</td>
</tr>
</tbody>
</table>

* Piperacillin and tazobactam are present in the formulation as sodium salts. Dextrose hydrous,
sodium citrate dihydrate, and edetate disodium dihydrate amounts are approximate.

ZOSYN contains a total of 2.84 mEq (65 mg) of sodium (Na\(^+\)) per gram of piperacillin in the
combination product.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

ZOSYN is an antibacterial drug [see Microbiology (12.4)].

12.2 Pharmacodynamics

The pharmacodynamic parameter for piperacillin/tazobactam that is most predictive of clinical and
microbiological efficacy is time above MIC.

12.3 Pharmacokinetics

The mean and coefficients of variation (CV\%) for the pharmacokinetic parameters of piperacillin and
tazobactam after multiple intravenous doses are summarized in Table 6.

Table 6: Mean (CV\%) Piperacillin and Tazobactam PK Parameters

<table>
<thead>
<tr>
<th>Piperacillin/Tazobactam Dose(^*)</th>
<th>(C_{max}) mcg/mL</th>
<th>AUC(^+) mcg·h/mL</th>
<th>CL mL/min</th>
<th>(V) L</th>
<th>(T_{1/2}) h</th>
<th>CL(_R) mL/min</th>
</tr>
</thead>
</table>
Peak plasma concentrations of piperacillin and tazobactam are attained immediately after completion of an intravenous infusion of ZOSYN. Piperacillin plasma concentrations, following a 30-minute infusion of ZOSYN, were similar to those attained when equivalent doses of piperacillin were administered alone. Steady-state plasma concentrations of piperacillin and tazobactam were similar to those attained after the first dose due to the short half-lives of piperacillin and tazobactam.

Distribution

Both piperacillin and tazobactam are approximately 30% bound to plasma proteins. The protein binding of either piperacillin or tazobactam is unaffected by the presence of the other compound. Protein binding of the tazobactam metabolite is negligible.

Piperacillin and tazobactam are widely distributed into tissues and body fluids including intestinal mucosa, gallbladder, lung, female reproductive tissues (uterus, ovary, and fallopian tube), interstitial fluid, and bile. Mean tissue concentrations are generally 50% to 100% of those in plasma. Distribution of piperacillin and tazobactam into cerebrospinal fluid is low in subjects with non-inflamed meninges, as with other penicillins (see Table 7).

### Table 7: Piperacillin/Tazobactam Concentrations in Selected Tissues and Fluids after Single 4 g/0.5 g 30-min IV Infusion of ZOSYN

<table>
<thead>
<tr>
<th>Tissue or Fluid</th>
<th>N*</th>
<th>Sampling period (h)</th>
<th>Mean PIP Concentration (mg/L)</th>
<th>Tissue:Plasma Range</th>
<th>Mean Tazo Concentration (mg/L)</th>
<th>Tissue:Tazo Concentration Range</th>
<th>Tazo CL (mL/min)</th>
<th>Tissue V (L)</th>
<th>T/2 (h)</th>
<th>CLR (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>35</td>
<td>0.5 – 4.5</td>
<td>34.8 – 94.2</td>
<td>0.60 – 1.1</td>
<td>4.0 – 7.7</td>
<td>0.49 – 0.93</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatty Tissue</td>
<td>37</td>
<td>0.5 – 4.5</td>
<td>4.0 – 10.1</td>
<td>0.097 – 0.115</td>
<td>0.7 – 1.5</td>
<td>0.10 – 0.13</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle</td>
<td>36</td>
<td>0.5 – 4.5</td>
<td>9.4 – 23.3</td>
<td>0.29 – 0.18</td>
<td>1.4 – 2.7</td>
<td>0.18 – 0.30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal Intestinal Mucosa</td>
<td>7</td>
<td>1.5 – 2.5</td>
<td>31.4</td>
<td>0.55</td>
<td>10.3</td>
<td>1.15</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal Intestinal Mucosa</td>
<td>7</td>
<td>1.5 – 2.5</td>
<td>31.2</td>
<td>0.59</td>
<td>14.5</td>
<td>2.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appendix</td>
<td>22</td>
<td>0.5 – 2.5</td>
<td>26.5 – 64.1</td>
<td>0.43 – 0.53</td>
<td>9.1 – 18.6</td>
<td>0.80 – 1.35</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Each subject provided a single sample.
† Time from the start of the infusion
Piperacillin is metabolized to a minor microbiologically active desethyl metabolite. Tazobactam is metabolized to a single metabolite that lacks pharmacological and antibacterial activities.

Excretion

Following single or multiple ZOSYN doses to healthy subjects, the plasma half-life of piperacillin and of tazobactam ranged from 0.7 to 1.2 hours and was unaffected by dose or duration of infusion.

Both piperacillin and tazobactam are eliminated via the kidney by glomerular filtration and tubular secretion. Piperacillin is excreted rapidly as unchanged drug with 68% of the administered dose excreted in the urine. Tazobactam and its metabolite are eliminated primarily by renal excretion with 80% of the administered dose excreted as unchanged drug and the remainder as the single metabolite. Piperacillin, tazobactam and desethyl piperacillin are also secreted into the bile.

Specific Populations

Renal Impairment

After the administration of single doses of piperacillin/tazobactam to subjects with renal impairment, the half-life of piperacillin and of tazobactam increases with decreasing creatinine clearance. At creatinine clearance below 20 mL/min, the increase in half-life is twofold for piperacillin and fourfold for tazobactam compared to subjects with normal renal function. Dosage adjustments for ZOSYN are recommended when creatinine clearance is below 40 mL/min in patients receiving the usual recommended daily dose of ZOSYN. See Dosage and Administration (2) for specific recommendations for the treatment of patients with renal impairment.

Hemodialysis removes 30% to 40% of a piperacillin/tazobactam dose with an additional 5% of the tazobactam dose removed as the tazobactam metabolite. Peritoneal dialysis removes approximately 6% and 21% of the piperacillin and tazobactam doses, respectively, with up to 16% of the tazobactam dose removed as the tazobactam metabolite. For dosage recommendations for patients undergoing hemodialysis [see Dosage and Administration (2)].

Hepatic Impairment

The half-life of piperacillin and of tazobactam increases by approximately 25% and 18%, respectively, in patients with hepatic cirrhosis compared to healthy subjects. However, this difference does not warrant dosage adjustment of ZOSYN due to hepatic cirrhosis.

Pediatrics

Piperacillin and tazobactam pharmacokinetics were studied in pediatric patients 2 months of age and older. The clearance of both compounds is slower in the younger patients compared to older children and adults.

In a population PK analysis, estimated clearance for 9 month-old to 12 year-old patients was comparable to adults, with a population mean (SE) value of 5.64 (0.34) mL/min/kg. The piperacillin clearance estimate is 80% of this value for pediatric patients 2 – 9 months old. In patients younger than 2 months of age, clearance of piperacillin is slower compared to older children; however, it is not adequately characterized for dosing recommendations. The population mean (SE) for piperacillin distribution volume is 0.243 (0.011) L/kg and is independent of age.

Geriatrics

The impact of age on the pharmacokinetics of piperacillin and tazobactam was evaluated in healthy male subjects, aged 18 – 35 years (n=6) and aged 65 to 80 years (n=12). Mean half-life for piperacillin and tazobactam was 32% and 55% higher, respectively, in the elderly compared to the younger subjects. This difference may be due to age-related changes in creatinine clearance.

Race

The effect of race on piperacillin and tazobactam was evaluated in healthy male volunteers. No difference in piperacillin or tazobactam pharmacokinetics was observed between Asian (n=9) and
Caucasian (n=9) healthy volunteers who received single 4/0.5 g doses.

Drug Interactions

The potential for pharmacokinetic drug interactions between ZOSYN and aminoglycosides, probenecid, vancomycin, heparin, vecuronium, and methotrexate has been evaluated [see Drug Interactions (7)].

12.4 Microbiology

Mechanism of Action

Piperacillin sodium exerts bactericidal activity by inhibiting septum formation and cell wall synthesis of susceptible bacteria. *In vitro*, piperacillin is active against a variety of Gram-positive and Gram-negative aerobic and anaerobic bacteria. Tazobactam sodium has little clinically relevant *in vitro* activity against bacteria due to its reduced affinity to penicillin-binding proteins. It is, however, a β-lactamase inhibitor of the Molecular class A enzymes, including Richmond-Sykes class III (Bush class 2b & 2b') penicillinases and cephalosporinases. It varies in its ability to inhibit class II and IV (2a & 4) penicillinases. Tazobactam does not induce chromosomally-mediated β-lactamases at tazobactam concentrations achieved with the recommended dosage regimen.

Spectrum of Activity

Piperacillin/tazobactam has been shown to be active against most isolates of the following microorganisms both *in vitro* and in clinical infections [see Indications and Usage (1)].

Gram-positive bacteria:

*Staphylococcus aureus* (methicillin susceptible isolates only)

Gram-negative bacteria:

*Acinetobacter baumannii*

*Escherichia coli*

*Haemophilus influenzae* (excluding β-lactamase negative, ampicillin-resistant isolates)

*Klebsiella pneumoniae*

*Pseudomonas aeruginosa* (given in combination with an aminoglycoside to which the isolate is susceptible)

Anaerobic bacteria:

*Bacteroides fragilis* group (*B. fragilis, B. ovatus, B. thetaiotaomicron, and B. vulgatus*)

The following *in vitro* data are available, but their clinical significance is unknown.

At least 90% of the following microorganisms exhibit an *in vitro* minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for piperacillin/tazobactam. However, the safety and effectiveness of piperacillin/tazobactam in treating clinical infections due to these bacteria have not been established in adequate and well-controlled clinical trials.

Gram-positive bacteria:

*Enterococcus faecalis* (ampicillin or penicillin-susceptible isolates only)

*Staphylococcus epidermidis* (methicillin susceptible isolates only)

*Streptococcus agalactiae*²

*Streptococcus pneumoniae*² (penicillin-susceptible isolates only)

*Streptococcus pyogenes*²

Viridans group streptococci²

Gram-negative bacteria:

*Citrobacter koseri*

*Moraxella catarrhalis*

*Morganella morganii*
Morganella morganii
*Neisseria gonorrhoeae*
*Proteus mirabilis*
*Proteus vulgaris*
*Serratia marcescens*
*Providencia stuartii*
*Providencia rettgeri*
*Salmonella enterica*

Anaerobic bacteria:

*Clostridium perfringens*
*Bacteroides distasonis*
*Prevotella melaninogenica*

2 These are not β-lactamase producing bacteria and, therefore, are susceptible to piperacillin alone.

Susceptibility Testing

For specific information regarding susceptibility test interpretive criteria and associated test methods and quality control standards recognized by FDA for this drug, please see: https://www.fda.gov/STIC.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term carcinogenicity studies in animals have not been conducted with piperacillin/tazobactam, piperacillin, or tazobactam.

Piperacillin/Tazobactam

Piperacillin/tazobactam was negative in microbial mutagenicity assays, the unscheduled DNA synthesis (UDS) test, a mammalian point mutation (Chinese hamster ovary cell HPRT) assay, and a mammalian cell (BALB/c-3T3) transformation assay. *In vivo*, piperacillin/tazobactam did not induce chromosomal aberrations in rats.

*Piperacillin/tazobactam*

Reproduction studies have been performed in rats and have revealed no evidence of impaired fertility when piperacillin/tazobactam is administered intravenously up to a dose of 1280/320 mg/kg piperacillin/tazobactam, which is similar to the maximum recommended human daily dose based on body-surface area (mg/m²).

15 REFERENCES


CLINITEST® is a registered trademark of Siemens Healthcare Diagnostics Inc.

GALAXY is a registered trademark of Baxter International Inc.

16 HOW SUPPLIED/STORAGE AND HANDLING

ZOSYN (piperacillin and tazobactam) for Injection are supplied as single-dose vials and pharmacy bulk vials in the following sizes:

- Each ZOSYN 2.25 g vial provides piperacillin sodium equivalent to 2 grams of piperacillin and tazobactam sodium equivalent to 0.25 g of tazobactam. Each vial contains 5.68 mEq (130 mg) of sodium. Supplied 10 per box—NDC 0206-8852-16
- Each ZOSYN 3.375 g vial provides piperacillin sodium equivalent to 3 grams of piperacillin and
tazobactam sodium equivalent to 0.375 g of tazobactam. Each vial contains 8.52 mEq (195 mg) of sodium. Supplied 10 per box—NDC 0206-8854-16
- Each ZOSYN 4.5 g vial provides piperacillin sodium equivalent to 4 grams of piperacillin and tazobactam sodium equivalent to 0.5 g of tazobactam. Each vial contains 11.36 mEq (260 mg) of sodium. Supplied 10 per box—NDC 0206-8855-16
- Each ZOSYN 40.5 g pharmacy bulk vial provides piperacillin sodium equivalent to 36 grams of piperacillin and tazobactam sodium equivalent to 4.5 grams of tazobactam. Each pharmacy bulk vial contains 100.4 mEq (2,304 mg) of sodium. NDC 0206-8859-10

ZOSYN for Injection vials should be stored at controlled room temperature (20°C to 25°C [68°F to 77°F]) prior to reconstitution.

ZOSYN (piperacillin and tazobactam) Injection in GALAXY Containers are supplied as a frozen, iso-osmotic, sterile, nonpyrogenic solution in single dose plastic containers as follows:
- 2.25 g (piperacillin sodium equivalent to 2 g piperacillin/tazobactam sodium equivalent to 0.25 g tazobactam) in 50 mL. Each container has 5.58 mEq (128 mg) of sodium. Supplied 24/box—NDC 0206-8860-02
- 3.375 g (piperacillin sodium equivalent to 3 g piperacillin/tazobactam sodium equivalent to 0.375 g tazobactam) in 50 mL. Each container has 8.38 mEq (192 mg) of sodium. Supplied 24/box—NDC 0206-8861-02
- 4.5 g (piperacillin sodium equivalent to 4 g piperacillin/tazobactam sodium equivalent to 0.5 g tazobactam) in 100 mL. Each container has 11.17 mEq (256 mg) of sodium. Supplied 12/box—NDC 0206-8862-02

ZOSYN Injection in GALAXY Containers should be stored at or below -20°C (-4°F).

17 PATIENT COUNSELING INFORMATION

Serious Hypersensitivity Reactions
Advise patients, their families, or caregivers that serious hypersensitivity reactions, including serious allergic cutaneous reactions, could occur that require immediate treatment. Ask them about any previous hypersensitivity reactions to ZOSYN, other beta-lactams (including cephalosporins), or other allergens [see Warnings and Precautions (5.2)].

Diarrhea
Advise patients, their families, or caregivers that diarrhea is a common problem caused by antibacterial drugs which usually ends when the drug is discontinued. Sometimes after starting treatment with antibacterial drugs, 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 drug. If this occurs, patients should contact their physician as soon as possible.

Antibacterial Resistance
Counsel patients that antibacterial drugs including ZOSYN should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When ZOSYN 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 ZOSYN or other antibacterial drugs in the future.

Counsel patients that ZOSYN can cross the placenta in humans and is excreted in human milk.
This product's label may have been updated. For current package insert and further product information, please visit http://www.pfizer.com or call our medical communications department toll-free at 1-800-438-1985.

PRINCIPAL DISPLAY PANEL - 2.25 gram Vial Label
NDC 0206-8852-08
2.25 gram Single Use Vial
Zosyn®
(piperacillin and tazobactam) for injection
2.25 gram
For IV Use Only
Rx only

PRINCIPAL DISPLAY PANEL - 2.25 gram Vial Carton
NDC 0206-8852-16
Contains 10 vials of
NDC 0206-8852-08
Rx only
10 x 2.25 gram Single Use Vials
Zosyn®
(piperacillin and tazobactam for injection, USP)

2.25 gram
For IV Use Only

Pfizer Injectables
10 x 2.25 gram Single Use Vials

Zosyn®
(piperacillin and tazobactam for injection, USP)

2.25 gram
For IV Use Only

Pfizer Injectables
PACKAGE LABEL - PRINCIPAL DISPLAY PANEL - 2.25 G SINGLE DOSE CONTAINER

NDC 0206-8860-01

ZOSYN®
(Piperacillin and Tazobactam Injection)

2.25 g

GALAXY
Single Dose Container

50 mL

Iso-osmotic
Sterile Nonpyrogenic

Rx only
ZOSYN®
(Piperacillin and Tazobactam Injection)
2.25 g
Rx only

GALAXY
Single Dose Container
50 mL
Iso-osmotic
Sterile Nonpyrogenic

Store at or below -20°C/-4°F. Thaw at room temperature 20°C to 25°C (68°F to 77°F) or under refrigeration 2°C to 8°C (36°F to 46°F). DO NOT FORCE THAW BY IMMERSION IN WATER BATHS OR BY MICROWAVE IRRADIATION. Thawed solution remains stable for 14 days under refrigeration or 24 hours at room temperature.

Do not refreeze.

Dosage and Use: For intravenous use only. As directed by a physician. See Package Insert. Cautions: Do not add supplementary medication or additives. Must not be used in series connections. Check for minute leaks and solution clarity.

Each 50 mL contains: Piperacillin Sodium equivalent to 2 g Piperacillin and Tazobactam Sodium equivalent to 0.25 g Tazobactam in Water for Injection. Approximately 1 g Dextrose Hydrate added to adjust osmolality. Approximately 100 mg Sodium Citrate Dihydrate added as a buffer, pH adjusted with sodium bicarbonate and hydrochloric acid. pH 5.5 - 6.8

Each 50 mL also contains approximately 0.5 mg Edetate Disodium Dihydrate added as a metal chelator.

GALAXY is a registered trademark of Baxter International Inc.

Distributed by
Wyeth Pharmaceuticals Inc.
A subsidiary of Pfizer Inc.
Philadelphia, PA 19101

PL 2040 Plastic PA0023036
07-3-4-65-953
PRINCIPAL DISPLAY PANEL - 2.25 g Bag Box

ZOSYN®
(Piperacillin and Tazobactam Injection)

Rx only

2.25 g

2 x 12 x 50 mL Single Dose Containers
Contains 2 boxes of 12 of NDC 0206-8860-01

Iso-osmotic
Store at or below -20°C/-4°F.
Do not refreeze.

NDC 0206-8860-02
Contains 24 of NDC 0206-8860-01
Code 2G3575

Pfizer Injectables
PRINCIPAL DISPLAY PANEL - 3.375 gram Vial Label
NDC 0206-8854-08
3.375 gram Single Use Vial
Zosyn®
(piperacillin and tazobactam) for injection
3.375 gram
For IV Use Only
Rx only

PRINCIPAL DISPLAY PANEL - 3.375 gram Vial Carton
NDC 0206-8854-16
Contains 10 vials of
NDC 0206-8854-08
Rx only
10 x 3.375 gram Single Use Vials
Zosyn®
(piperacillin and tazobactam for injection, USP)
3.375 gram
For IV Use Only
Pfizer Injectables
10 x 3.375 gram Single Use Vials

**Zosyn®**
(piperacillin and tazobactam for injection, USP)

**3.375 gram**

For IV Use Only

**Pfizer Injectables**
10 x 3.375 gram Single Use Vials

Zosyn®
(piperacillin and tazobactam for injection, USP)

3.375 gram

For IV Use Only

Pfizer Injectables
NDC 0206-8861-01
ZOSYN®
(Piperacillin and Tazobactam Injection)
3.375 g
GALAXY
Single Dose Container
50 mL
Iso-osmotic
Sterile Nonpyrogenic
Rx only
ZOSYN® (Piperacillin and Tazobactam Injection) 3.375 g

Rx only

GALAXY 50 mL Iso-osmotic

Single Dose Container

Store at or below 20°C to 25°C (68°F to 77°F) or under refrigeration 2°C to 8°C (36°F to 46°F). DO NOT FORCE THAW BY IMMERSION IN WATER BATHS OR BY MICROWAVE IRRADIATION. Thawed solution remains stable for 14 days under refrigeration or 24 hours at room temperature.

Do not refreeze.

Condition: For intravenous use only. As directed by a physician. See Package Insert.

Cautions: Do not add supplementary medication or additives. Must not be used in series connections. Check for minute leaks and solution clarity.

Each 50 mL contains: Piperacillin Sodium equivalent to 3 g Piperacillin and Tazobactam Sodium equivalent to 0.375 g Tazobactam in Water for Injection. Approximately 350 mg Dextrose Hydrate added to adjust osmolality. Approximately 150 mg Sodium Citrate Dihydrate added as a buffer, pH adjusted with sodium bicarbonate and hydrochloric acid. pH 5.5 - 6.8

Each 50 mL also contains approximately 0.75 mg Edetate Disodium Dihydrate added as a metal chelator.

GALAXY is a registered trademark of Baxter International Inc.

Distributed by Wyeth Pharmaceuticals Inc. in association with Pfizer Inc.

Philadelphia, PA 19101

PL 2040 Plastic
PA4023037
O7:34 65-954
PRINCIPAL DISPLAY PANEL - 3.375 g Bag Box

ZOSYN®
(Piperacillin and Tazobactam Injection)

Rx only

3.375 g

2 x 12 x 50 mL Single Dose Containers
Contains 2 boxes of 12 of NDC 0206-8861-01
Iso-osmotic
Store at or below -20°C/-4°F.
Do not refreeze.

NDC 0206-8861-02
Contains 24 of NDC 0206-8861-01
Code 2G3576

Pfizer Injectables
**GALAXY Container**

Sterile Nonpyrogenic

Each 50 mL contains: Piperacillin Sodium equivalent to 3 g Piperacillin and Tazobactam Sodium equivalent to 0.375 g Tazobactam in Water for Injection. Approximately 350 mg Dextrose Hydrate added to adjust osmolality. Approximately 150 mg Sodium Chloride Dihydrate added as a buffer, pH adjusted with sodium bicarbonate and hydrochloric acid, pH 5.5 - 6.8

Each 50 mL also contains approximately 0.75 mg Edetate Disodium Dihydrate added as a metal chelator.

Dosage and Use: For Intravenous use only. As directed by a physician. See package insert.

Cautions: Do not add supplementary medications or additives. Must not be used in series connections. Check for minute leaks by squeezing thawed bag firmly. If leaks are found, discard bag as stability may be impaired. Do not use unless solution is clear.

---

**ZOSYN**

(Piperacillin and Tazobactam Injection)

Rx only

3.375g

Pfizer Injectables

2 x 12 x 50 mL Single Dose Containers

Contains 2 boxes of 12 of NDC 0206-8861-01

Iso-thermal

Store at or below -20°C/-4°F.

Do not re-freeze.

NO COPY

NO TEXT

NO VARNISH

Thaw at room temperature 20° to 25°C (68° to 77°F) or under refrigeration 2° to 8°C (36° to 46°F). DO NOT FORCE THAW BY IMMERSION IN WATER BATHS OR BY MICROWAVE IRRADIATION. Thawed solution remains sterile for 14 days under refrigeration 2° to 8°C (36° to 46°F) or 24 hours at room temperature 20° to 25°C (68° to 77°F). Do not re-freeze.

GALAXY is a registered trademark of Baxter International Inc.

Distributed by

Wyeth Pharmaceuticals Inc.

A subsidiary of Pfizer Inc

Philadelphia, PA 19101

GTIN: 00302068881020

07-04-75-620

---

NDC 0206-8855-08

PRINCIPAL DISPLAY PANEL - 4.5 gram Vial Label
4.5 gram Single Use Vial

Zosyn®
(piperacillin and tazobactam) for injection

4.5 gram

For IV Use Only

Rx only

This is an image of the principal display panel for a 4.5 gram Single Use Vial of Zosyn® (piperacillin and tazobactam) for injection. It contains 10 of NDC 0206-8855-08. The product is for IV Use Only and requires a prescription (Rx only).

PRINCIPAL DISPLAY PANEL - 4.5 gram Vial Carton

NDC 0206-8855-16
Contains 10 of
NDC 0206-8855-08
Rx only

10 x 4.5 gram Single Use Vials

Zosyn®
(piperacillin and tazobactam for Injection, USP)

4.5 gram

For IV Use Only

Pfizer Injectables
Zosyn®
(piperacillin and tazobactam for Injection, USP)
4.5 gram
For IV Use Only

Pfizer Injectables
ZOSYN®
(Piperacillin and Tazobactam Injection)
4.5 g
GALAXY
Single Dose Container
100 mL
Iso-osmotic
Sterile Nonpyrogenic
Rx only
Store at or below -20° C to 4° F. Thaw at room temperature 20° to 25° C (68° to 77° F)
or under refrigeration 2° to 8° C (36° to 46° F). Do not freeze. Do not thaw by immersion
in water baths or by microwave irradiation. Thawed solution remains
stable for 14 days under refrigeration or 24 hours at room temperature.

Dosage and Use: For intravenous use only. As directed by a physician. See Package Insert.
Cautions: Do not add supplementary medication or additives. Must not be used
in series connections. Check for minute leaks and solution clarity.

Each 100 mL contains: Piperacillin Sodium equivalent to 4 g Piperacillin and
Tazobactam Sodium equivalent to 0.5 g Tazobactam in Water for Injection.
Approximately 2 g Dextrose Hydrate added to adjust osmolality. Approximately
200 mg Sodium Citrate Dihydrate added as a buffer, pH adjusted with sodium
bicarbonate and hydrochloric acid, pH 5.5 - 6.8
Each 100 mL also contains approximately 1 mg Edetate Disodium Dihydrate added
as a metal chelator.
PRINCIPAL DISPLAY PANEL - 4.5 g Bag Box

ZOSYN®
(Piperacillin and Tazobactam Injection)
Rx only
4.5 g
2 x 6 x 100 mL Single Dose Containers
Contains 2 boxes of 6 of NDC 0206-8862-01
Iso-osmotic
Store at or below -20°C/-4°F.
Do not refreeze.
NDC 0206-8862-02
Contains 12 of NDC 0206-8862-01
Code 2G3577
Pfizer Injectables
Zosyn®
Rx only

(Piperacillin and Tazobactam for Injection, USP)

40.5 gram vial

PHARMACY BULK PACKAGE
Not for Direct Infusion

Distributed by Wyeth Pharmaceuticals Inc
A subsidiary of Pfizer Inc, Philadelphia, PA 19101

PRINCIPAL DISPLAY PANEL - 40.5 gram Vial Carton

NDC 0206-8859-10
Rx only
Zosyn®
(Piperacillin and Tazobactam for Injection, USP)
40.5 gram vial
PHARMACY BULK PACKAGE
Not for Direct Infusion
RECONSTITUTED STOCK SOLUTION MUST BE TRANSFERRED AND FURTHER DILUTED
FOR I.V. INFUSION

*Pfizer Injectables*
Zosyn®
(Piperacillin and Tazobactam for Injection, USP)
40.5 gram vial
PHARMACY BULK PACKAGE
Not for Direct Infusion
RECONSTITUTED STOCK SOLUTION MUST BE TRANSFERRED AND FURTHER DILUTED FOR IV, INFUSION
Pfizer Injectables

Zosyn®
(Piperacillin and Tazobactam for Injection, USP)
40.5 gram vial
PHARMACY BULK PACKAGE
Not for Direct Infusion
RECONSTITUTED STOCK SOLUTION MUST BE TRANSFERRED AND FURTHER DILUTED FOR IV, INFUSION
Pfizer Injectables

WLS 282
Zosyn®
(Piperacillin and Tazobactam for Injection, USP)
40.5 gram vial

PHARMACY BULK PACKAGE
Not for Direct Infusion

RECONSTITUTED STOCK SOLUTION MUST BE TRANSFERRED AND FURTHER DILUTED FOR I.V. INFUSION

Does not contain preservatives. Reconstitute with exactly 152 mL of a suitable diluent to achieve a concentration of 200 mg/mL of piperacillin and 25 mg/mL of tazobactam. Discard any unused portion after 24 hours if stored at room temperature or after 48 hours if refrigerated. See package insert for complete directions for use.

Prior to Reconstitution: Store at controlled room temperature 20° to 25°C (68° to 77°F).

After Reconstitution: Do not freeze. Reconstituted solution, See package insert for stability of reconstituted solution.

Contains piperacillin and tazobactam cryodesiccated powders for injection equivalent to 36 grams of piperacillin, 4.5 grams of tazobactam and 100.4 mEq (2.304 mg) of sodium. Contains 9 mg of edetate disodium dihydrate.

Distributed by
Wyeth Pharmaceuticals Inc
A subsidiary of Pfizer Inc
Philadelphia, PA 19101
**ZOSYN**
piperacillin sodium and tazobactam sodium injection, powder, lyophilized, for solution

### Product Information

<table>
<thead>
<tr>
<th>Product Type</th>
<th>Item Code (Source)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HUMAN PRESCRIPTION DRUG</td>
<td>NDC:0206-8854</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Route of Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTRAVENOUS</td>
</tr>
</tbody>
</table>

#### Active Ingredient/Active Moiety

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAZOBACTAM SODIUM (UNII: UXA545ABTT) (TAZOBACTAM - UNII:SE10G96M8W)</td>
<td>TAZOBACTAM</td>
<td>0.375 g in 15 mL</td>
</tr>
<tr>
<td>PIPERACILLIN SODIUM (UNII: M98T69Q7HP) (PIPERACILLIN ANHYDROUS - UNII99E28532GX)</td>
<td>PIPERACILLIN ANHYDROUS</td>
<td>3 g in 15 mL</td>
</tr>
</tbody>
</table>

#### Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>SODIUM CITRATE, UNSPECIFIED FORM (UNII: IQ73QZJULR)</td>
<td></td>
</tr>
<tr>
<td>EDETATE DISODIUM (UNII: 7FLD91C86K)</td>
<td>0.75 mg in 15 mL</td>
</tr>
</tbody>
</table>

### Packaging

<table>
<thead>
<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NDC:0206-8854-16</td>
<td>10 in 1 CARTON</td>
<td>11/01/1993</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>NDC:0206-8854-08</td>
<td>15 mL in 1 VIAL, SINGLE-USE; Type 0: Not a Combination Product</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Marketing Information

<table>
<thead>
<tr>
<th>Marketing Category</th>
<th>Application Number or Monograph Citation</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDA</td>
<td>NDA050684</td>
<td>11/01/1993</td>
<td></td>
</tr>
</tbody>
</table>
### ZOSYN
piperacillin sodium and tazobactam sodium injection, powder, lyophilized, for solution

#### Product Information

<table>
<thead>
<tr>
<th>Product Type</th>
<th>HUMAN PRESCRIPTION DRUG</th>
<th>Item Code (Source)</th>
<th>NDC:0206-8852</th>
</tr>
</thead>
<tbody>
<tr>
<td>Route of Administration</td>
<td>INTRAVENOUS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Active Ingredient/Active Moiety

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAZOBACTAM SODIUM (UNII: UXA545ABTT) (TAZOBACTAM - UNII:SE10G96M8W)</td>
<td>TAZOBACTAM</td>
<td>0.25 g in 10 mL</td>
</tr>
<tr>
<td>PIPERACILLIN SODIUM (UNII: M98T69Q7HP) (PIPERACILLIN ANHYDROUS - UNII:9I628532GX)</td>
<td>PIPERACILLIN ANHYDROUS</td>
<td>2 g in 10 mL</td>
</tr>
</tbody>
</table>

#### Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>SODIUM CITRATE, UNSPECIFIED FORM (UNII: 1Q73Q2JULR)</td>
<td></td>
</tr>
<tr>
<td>EDETATE DISODIUM (UNII: 7FLD91IC86K)</td>
<td>0.5 mg in 10 mL</td>
</tr>
</tbody>
</table>

#### Packaging

<table>
<thead>
<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NDC:0206-8852-16</td>
<td>10 in 1 CARTON</td>
<td>11/01/1993</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>NDC:0206-8852-08</td>
<td>10 mL in 1 VIAL, SINGLE-USE; Type 0: Not a Combination Product</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Marketing Information

<table>
<thead>
<tr>
<th>Marketing Category</th>
<th>Application Number or Monograph Citation</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDA</td>
<td>NDA050684</td>
<td>11/01/1993</td>
<td></td>
</tr>
</tbody>
</table>

---

### ZOSYN
piperacillin sodium and tazobactam sodium injection, powder, lyophilized, for solution

#### Product Information

<table>
<thead>
<tr>
<th>Product Type</th>
<th>HUMAN PRESCRIPTION DRUG</th>
<th>Item Code (Source)</th>
<th>NDC:0206-8855</th>
</tr>
</thead>
<tbody>
<tr>
<td>Route of Administration</td>
<td>INTRAVENOUS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Active Ingredient/Active Moiety

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TAZOBACTAM SODIUM</strong> (UNII: UXA545ABTT) (TAZOBACTAM - UNII:SE10G96MBW)</td>
<td>TAZOBACTAM</td>
<td>0.5 g in 20 mL</td>
</tr>
<tr>
<td><strong>PIPERACILLIN SODIUM</strong> (UNII: M98T69Q7HP) (PIPERACILLIN ANHYDROUS - UNII:9I628532GX)</td>
<td>PIPERACILLIN ANHYDROUS</td>
<td>4 g in 20 mL</td>
</tr>
</tbody>
</table>

### Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SODIUM CITRATE, UNSPECIFIED FORM</strong> (UNII: 1Q73Q2JULR)</td>
<td></td>
</tr>
<tr>
<td><strong>EDETATE DISODIUM</strong> (UNII: 7FLD91C86K)</td>
<td>1 mg in 20 mL</td>
</tr>
</tbody>
</table>

### Packaging

<table>
<thead>
<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NDC:0206-8855-16</td>
<td>10 in 1 CARTON</td>
<td>11/01/1993</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>NDC:0206-8855-08</td>
<td>20 mL in 1 VIAL, SINGLE-USE; Type 0: Not a Combination Product</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Marketing Information

<table>
<thead>
<tr>
<th>Marketing Category</th>
<th>Application Number or Monograph Citation</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDA</td>
<td>NDA050684</td>
<td>11/01/1993</td>
<td></td>
</tr>
</tbody>
</table>

### ZOSYN  PHARMACY BULK PACKAGE

piperacillin sodium and tazobactam sodium injection, powder, lyophilized, for solution

### Product Information

<table>
<thead>
<tr>
<th>Product Type</th>
<th>Item Code (Source)</th>
<th>NDC:0206-8859</th>
</tr>
</thead>
<tbody>
<tr>
<td>HUMAN PRESCRIPTION DRUG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>INTRAVENOUS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Active Ingredient/Active Moiety

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TAZOBACTAM SODIUM</strong> (UNII: UXA545ABTT) (TAZOBACTAM - UNII:SE10G96MBW)</td>
<td>TAZOBACTAM</td>
<td>4.5 g in 180 mL</td>
</tr>
<tr>
<td><strong>PIPERACILLIN SODIUM</strong> (UNII: M98T69Q7HP) (PIPERACILLIN ANHYDROUS - UNII:9I628532GX)</td>
<td>PIPERACILLIN ANHYDROUS</td>
<td>36 g in 180 mL</td>
</tr>
</tbody>
</table>

### Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SODIUM CITRATE, UNSPECIFIED FORM</strong> (UNII: 1Q73Q2JULR)</td>
<td></td>
</tr>
<tr>
<td><strong>EDETATE DISODIUM</strong> (UNII: 7FLD91C86K)</td>
<td>9 mg in 180 mL</td>
</tr>
</tbody>
</table>
## Packaging

<table>
<thead>
<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NDC:0206-8859-10</td>
<td>1 in 1 CARTON</td>
<td></td>
<td>11/01/1993</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>180 mL in 1 VIAL, PHARMACY BULK PACKAGE; Type 0: Not a Combination Product</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Marketing Information

<table>
<thead>
<tr>
<th>Marketing Category</th>
<th>Application Number or Monograph Citation</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDA</td>
<td>NDA050684</td>
<td>11/01/1993</td>
<td></td>
</tr>
</tbody>
</table>

## ZOSYN IN GALAXY CONTAINERS
tazobactam sodium and piperacillin sodium injection, solution

## Product Information

<table>
<thead>
<tr>
<th>Product Type</th>
<th>HUMAN PRESCRIPTION DRUG</th>
<th>Item Code (Source)</th>
<th>NDC:0206-8860</th>
</tr>
</thead>
<tbody>
<tr>
<td>Route of Administration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>INTRAVENOUS</td>
</tr>
</tbody>
</table>

## Active Ingredient/Active Moiety

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAZOBACTAM SODIUM (UNII: UXA545ABTT) (TAZOBACTAM - UNII:SE10G96M8W)</td>
<td>TAZOBACTAM</td>
<td>250 mg in 50 mL</td>
</tr>
<tr>
<td>PIPERACILLIN SODIUM (UNII: M98T69Q7HP) (PIPERACILLIN ANHYDROUS - UNII:9I628532GX)</td>
<td>PIPERACILLIN ANHYDROUS</td>
<td>2 g in 50 mL</td>
</tr>
</tbody>
</table>

## Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEXTROSE MONOHYDRATE (UNII: LX22YL083G)</td>
<td>1 g in 50 mL</td>
</tr>
<tr>
<td>SODIUM CITRATE, UNSPECIFIED FORM (UNII: 1Q73Q2JULR)</td>
<td>100 mg in 50 mL</td>
</tr>
<tr>
<td>EDETADE DISODIUM (UNII: 7FLD91C86K)</td>
<td>0.5 mg in 50 mL</td>
</tr>
<tr>
<td>SODIUM BICARBONATE (UNII: 8MD55V39QO)</td>
<td></td>
</tr>
<tr>
<td>HYDROCHLORIC ACID (UNII: QTTI7582CB)</td>
<td></td>
</tr>
<tr>
<td>WATER (UNII: 059QF0KO0R)</td>
<td></td>
</tr>
</tbody>
</table>

## Packaging

<table>
<thead>
<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NDC:0206-8860-02</td>
<td>24 in 1 BOX</td>
<td>03/01/1998</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>NDC:0206-8860-01</td>
<td>50 mL in 1 BAG; Type 0: Not a Combination Product</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Marketing Information

<table>
<thead>
<tr>
<th>Marketing Category</th>
<th>Application Number or Monograph Citation</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDA</td>
<td>NDA050750</td>
<td>03/01/1998</td>
<td></td>
</tr>
</tbody>
</table>

### ZOSYN IN GALAXY CONTAINERS

tazobactam sodium and piperacillin sodium injection, solution

## Product Information

### Active Ingredient/Active Moiety

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAZOBACTAM SODIUM (UNII: UXA545ABTT) (TAZOBACTAM - UNII:SE10G96MBW)</td>
<td>TAZOBACTAM</td>
<td>375 mg in 50 mL</td>
</tr>
<tr>
<td>PIPERACILLIN SODIUM (UNII: M98T69Q7HP) (PIPERACILLIN ANHYDROUS - UNII:9I628532GX)</td>
<td>PIPERACILLIN ANHYDROUS</td>
<td>3 g in 50 mL</td>
</tr>
</tbody>
</table>

### Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEXTROSE MONOHYDRATE (UNII: LX22YL083G)</td>
<td>1.5 g in 50 mL</td>
</tr>
<tr>
<td>SODIUM CITRATE, UNSPECIFIED FORM (UNII: 1Q73Q2JULR)</td>
<td>150 mg in 50 mL</td>
</tr>
<tr>
<td>EDETADE DISODIUM (UNII: 7FLD91C86K)</td>
<td>0.75 mg in 50 mL</td>
</tr>
<tr>
<td>SODIUM BICARBONATE (UNII: 8MDF5V39QO)</td>
<td></td>
</tr>
<tr>
<td>HYDROCHLORIC ACID (UNII: QTT17582CB)</td>
<td></td>
</tr>
<tr>
<td>WATER (UNII: 059QF0KO0R)</td>
<td></td>
</tr>
</tbody>
</table>

### Packaging

<table>
<thead>
<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NDC:0206-8861-02</td>
<td>24 in 1 BOX</td>
<td>03/01/1998</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>NDC:0206-8861-01</td>
<td>50 mL in 1 BAG; Type 0: Not a Combination Product</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Marketing Information

<table>
<thead>
<tr>
<th>Marketing Category</th>
<th>Application Number or Monograph Citation</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDA</td>
<td>NDA050750</td>
<td>03/01/1998</td>
<td></td>
</tr>
<tr>
<td>Product Type</td>
<td>HUMAN PRESCRIPTION DRUG</td>
<td>Item Code (Source)</td>
<td>NDC:0206-8862</td>
</tr>
<tr>
<td>------------------------------</td>
<td>-------------------------</td>
<td>--------------------</td>
<td>---------------</td>
</tr>
<tr>
<td>Route of Administration</td>
<td>INTRAVENOUS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Active Ingredient/Active Moiety**

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAZOBACTAM SODIUM (UNII: UXA545ABTT) (TAZOBACTAM - UNII:SE10G96MBW)</td>
<td>TAZOBACTAM</td>
<td>500 mg in 100 mL</td>
</tr>
<tr>
<td>PIPERACILLIN SODIUM (UNII: M98T69Q7HP) (PIPERACILLIN ANHYDROUS - UNII:9I628532GX)</td>
<td>PIPERACILLIN ANHYDROUS</td>
<td>4 g in 100 mL</td>
</tr>
</tbody>
</table>

**Inactive Ingredients**

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEXTROSE MONOHYDRATE (UNII: LX22YL083G)</td>
<td>2 g in 100 mL</td>
</tr>
<tr>
<td>SODIUM CITRATE, UNSPECIFIED FORM (UNII: 1Q73Q2JULR)</td>
<td>200 mg in 100 mL</td>
</tr>
<tr>
<td>EDETATE DISODIUM (UNII: 7FLD91C86K)</td>
<td>1 mg in 100 mL</td>
</tr>
<tr>
<td>SODIUM BICARBONATE (UNII: 8MDF5V39QO)</td>
<td></td>
</tr>
<tr>
<td>HYDROCHLORIC ACID (UNII: QTT17582CB)</td>
<td></td>
</tr>
<tr>
<td>WATER (UNII: 059QF0KO0R)</td>
<td></td>
</tr>
</tbody>
</table>

**Packaging**

<table>
<thead>
<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NDC:0206-8862-02</td>
<td>12 in 1 BOX</td>
<td>03/01/1998</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>NDC:0206-8862-01</td>
<td>100 mL in 1 BAG; Type 0: Not a Combination Product</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Marketing Information**

<table>
<thead>
<tr>
<th>Marketing Category</th>
<th>Application Number or Monograph Citation</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDA</td>
<td>NDA050750</td>
<td>03/01/1998</td>
<td></td>
</tr>
</tbody>
</table>

**Labeler** - Wyeth Pharmaceuticals LLC, a subsidiary of Pfizer Inc. (113008515)

**Establishment**

- **Wyeth Lederle S.R.L.**
  - Name: Wyeth Lederle S.R.L.
  - Address: 542812040
  - ID/FEI: 113008515
  - Business Operations: ANALYSIS(0206-8862, 0206-8861, 0206-8860), LABEL(0206-8862, 0206-8861, 0206-8860), MANUFACTURE(0206-8862, 0206-8861, 0206-8860), PACK(0206-8862, 0206-8861, 0206-8860)

**Establishment**

- **Baxter Healthcare Corporation**
  - Name: Baxter Healthcare Corporation
  - Address: 194684502
  - ID/FEI: 113008515
  - Business Operations: ANALYSIS(0206-8862, 0206-8861, 0206-8860), LABEL(0206-8862, 0206-8861, 0206-8860), MANUFACTURE(0206-8862, 0206-8861, 0206-8860), PACK(0206-8862, 0206-8861, 0206-8860)

Revised: 5/2019