Grosyn-TZ Inj.
Piperacillin Sodium/Tazobactam Sodium for Injection

COMPOSITION
GROSYN-TZ INJ. 4.5 gm
Each vial contains
Piperacillin sodium equivalent to Piperacillin…….. 4gm
Tazobactam sodium equivalent to Tazobactam……. 500 mg

INDICATIONS
GROSYN-TZ INJ. is indicated for treatment of the following systemic and/or local bacterial infections in which susceptible organisms have been detected or are suspected:

Adults and the Elderly

- Lower respiratory tract infections
- Urinary tract infections (complicated and uncomplicated)
- Intra-abdominal infections including peritonitis and appendicitis complicated with rupture or abscess
- Skin and skin structure infections (complicated and uncomplicated)
- Post-partum endometritis and pelvic infections
- Polymicrobial infections
- Bacterial septicaemia
- Bacterial infections in neutropenic adults in combination with an aminoglycoside

Paediatrics

- Intra-abdominal infections including appendicitis complicated by rupture with peritonitis and/or abscess formation, biliary infections.
- Bacterial infections in neutropenic children in combination with an aminoglycoside.

Infections caused by piperacillin-susceptible organisms, for which piperacillin has been shown to be effective, are also amenable to piperacillin/ tazobactam treatment due to its piperacillin content. The tazobactam component of this combination product does not decrease the activity of the piperacillin component against piperacillin-susceptible organisms. Therefore, the treatment of mixed infections caused by piperacillin-susceptible organisms and piperacillin-resistant, beta-lactamase producing organisms susceptible to piperacillin /tazobactam should not require the addition of another antibiotic.

Piperacillin/Tazobactam is useful as presumptive therapy in the indicated conditions prior to the identification of causative organisms because of its broad spectrum of bactericidal activity against gram-positive and gram-negative aerobic and anaerobic organisms.

DOSAGE AND ADMINISTRATION
GROSYN-TZ INJ. should be administered by intravenous infusion over 20- 30 minutes.

Adolescents, Adults and Elderly with normal renal function

Total daily dose of **GROSYN-TZ INJ.** is 13.5g (12.0 g piperacillin/1.5 g tazobactam) in three to four equally divided doses.

Initial presumptive treatment of patients with nosocomial pneumonia and febrile neutropenia should start with **GROSYN-TZ INJ.** 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). Treatment with the aminoglycoside should be continued

in patients from whom *Pseudomonas aeruginosa* is isolated. If *Pseudomonas aeruginosa* is not isolated, the aminoglycoside may be discontinued at the discretion of the treating physician.

Paediatrics
GROSYN-TZ INJ. can be administered in paediatric patients above 2 months of age.
Intra-abdominal infections

- 2 months to 9 months of age: 80 mg piperacillin/10 mg tazobactam per kg q 8hr
- 9 months or older weighing upto 40 kg: 100mg piperacillin/12.5 mg tazobactam per kg q 8hr
- Weighing over 40 kg:- as per adult dose
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Neutropenia

- < 50 kg: 80 mg piperacillin/10 mg tazobactam per kg q 6 hr plus an aminoglycoside
- >50 kg: 4.5 g q 8 hr plus an aminoglycoside

Duration of Therapy

The usual duration of **GROSYN-TZ INJ.** treatment is from seven to ten days. However, the recommended duration of **GROSYN-TZ INJ.** treatment of nosocomial pneumonia is 7 to 14 days. In all conditions, the duration of therapy should be guided by the severity of the infection and the patient`s clinical and bacteriological progress.

Renal Insufficiency

In patients with renal insufficiency (creatinine clearance < 40 mL/min), the intravenous dose of**GROSYN-TZ INJ.** should be adjusted to the degree of actual renal function impairment. In patients with nosocomial pneumonia receiving concomitant aminoglycoside therapy, the aminoglycoside dosage should be adjusted according to the recommendations of the manufacturer. The recommended daily doses of **GROSYN-TZ INJ.** for patients with renal insufficiency are as follows:

Adults

Recommended Dosing of GROSYN-TZ INJ. in Patients with Normal Renal Function and Renal Insufficiency (As total grams piperacillin/tazobactam)		
Renal Function (Creatinine Clearance, mL/min)	**All Indications (except nosocomial pneumonia)**	**Nosocomial Pneumonia**
>40 mL/min	3.375 q 6 h	4.5 q 6 h
20-40 mL/min *	2.25 q 6 h	3.375 q 6 h
<20 mL/min *	2.25 q 8 h	2.25 q 6 h
Haemodialysis **	2.25 q 12 h	2.25 q 8 h
CAPD	2.25 q 12 h	2.25 q 8 h
* Creatinine clearance for patients not receiving haemodialysis		
** 0.75 g should be administered following each haemodialysis session on haemodialysis days		

For patients on haemodialysis, 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 haemodialysis removes 30% to 40% of the administered dose, an additional dose of 0.75 g **GROSYN-TZ INJ.** should be administered following each dialysis period on haemodialysis days. No additional dosage of **GROSYN-TZ INJ.** is necessary for CAPD patients.

Paediatrics

Creatinine Clearance (ml/min)	Recommended Piperacillin / Tazobactam Dosage
≥40	No adjustment
20-39	90mg (80mg piperacillin / 10mg tazobactam) /kg q 8H, not exceeding 13.5g/day
< 20	90mg (80mg piperacillin / 10mg tazobactam) /kg q 12H, not exceeding 9g/day

For children weighing < 50kg on haemodialysis the recommended dose is 45mg (40mg piperacillin /5mg tazobactam) /kg every 8 hours.

The above dosage modifications are only an approximation. Each patient must be monitored closely for signs of drug toxicity. Drug dose and interval should be adjusted accordingly.

Directions for reconstitution and dilution for use

Intravenous Administration

For conventional vials, reconstitute **GROSYN-TZ INJ.** per gram of piperacillin with 5 mL of a compatible reconstitution diluent from the list provided below.

4.5 g **GROSYN-TZ INJ.** should be reconstituted with 20 mL. When swirled constantly, reconstitution generally occurs within 5 to 10 minutes.

Use 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]).

Compatible Reconstitution Diluents

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
Intravenous injection should be given over at least 3-5 minutes.
Reconstituted **GROSYN-TZ INJ.** solution should be further diluted (recommended volume per dose of 50 mL to 150 mL) with a compatible intravenous diluent solution listed below. Administer by infusion over a period of at least 20-30 minutes. During the infusion it is desirable to discontinue the primary infusion solution.

Compatible Intravenous Diluent Solutions

0.9% Sodium Chloride for Injection
Sterile Water for Injection ‡
Dextrose 5%

Dextran 6% in Saline
‡ Maximum recommended volume per dose of Sterile Water for Injection is 50 mL.

CONTRAINDICATIONS

GROSYN-TZ INJ. is contraindicated in patients with a history of allergic reactions to any of the penicillins, cephalosporins, or beta-lactamase inhibitors.

PACKAGING INFORMATION

GROSYN-TZ INJ. 4.5 gm injection is available in vial of 30 mL ; with 20 ml of W.F.I.