# SUMMARY OF PRODUCT CHARACTERISTICS

$R_X$ Only

## 1. NAME OF PRODUCT: AUROTAZ-P 4.5.

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITIONS:

*Piperacillin and Tazobactam for Injection USP 4.5gm*
Each vial Contains:
Piperacillin Sodium USP equivalent to Piperacillin 4.0 gm and Tazobactam Sodium equivalent to Tazobactam USP 0.50 gm.

*For the full list of excipients, see section 6.1.*

## 3. PHARMACEUTICAL FORM:

**Dosage form:** Injection.

**Description:** White to off white crystalline powder.

## 4. CLINICAL PARTICULARS:

### 4.1 Therapeutic indications

Piperacillin and tazobactam is indicated for the treatment of the following infections in adults and children over 2 years of age:

***Adults and adolescents***
- Severe pneumonia including hospital-acquired and ventilator-associated pneumonia
- Complicated urinary tract infections (including pyelonephritis)
- Complicated intra-abdominal infections
- Complicated skin and soft tissue infections (including diabetic foot infections)

Treatment of patients with bacteraemia that occurs in association with, or is suspected to be associated with, any of the infections listed above.

Piperacillin and tazobactam may be used in the management of neutropenic patients with fever suspected to be due to a bacterial infection

***Children 2 to 12 years of age:***
- Complicated intra-abdominal infections

Piperacillin and tazobactam may be used in the management of neutropenic children with fever suspected to be due to a bacterial infection.
Consideration should be given to official guidance on the appropriate use of antibacterial agents.

### 4.2 Posology and method of administration Posology:

The dose and frequency of Piperacillin and tazobactam depends on the severity and localisation of the infection and expected pathogens.

***Adult and adolescent patients <u>Infections</u>***

The usual dose is 4 g piperacillin / 0.5 g tazobactam given every 8 hours.

For nosocomial pneumonia and bacterial infections in neutropenic patients, the recommended dose is 4 g piperacillin/0.5 g tazobactam administered every 6 hours. This regimen may also be applicable to treat patients with other indicated infections when particularly severe.

The following table summarises the treatment frequency and the recommended dose for adult and adolescent patients by indication or condition:

| **Treatment frequency** | **Piperacillin and Tazobactam 4 g / 0.5 g** |
|---|---|
| Every 6 hours | Severe pneumonia |
| | Neutropenic adults with fever suspected to be due to a bacterial infection |
| Every 8 hours | Complicated urinary tract infections (including pyelonephritis) |
| | Complicated intra-abdominal infections |
| | Skin and soft tissue infections (including diabetic foot infections) |

***<u>Patients with renal impairment</u>***

The intravenous dose should be adjusted to the degree of actual renal impairment as follows (each patient must be monitored closely for signs of substance toxicity; medicinal product dose and interval should be adjusted accordingly):

| **Creatinine Clearance** | **Piperacillin/Tazobactam Recommended** |
|---|---|

| **(ml/min)** | |
|---|---|
| > 40 | No dose adjustment necessary |
| 20-40 | Maximum dose suggested: 4 g / 0.5 g every 8 hours |
| < 20 | Maximum dose suggested: 4 g / 0.5 g every 12 hours |

For patients on haemodialysis, one additional dose of piperacillin / tazobactam 2 g / 0.25 g should be administered following each dialysis period, because haemodialysis removes 30%-50% of piperacillin in 4 hours.

***Patients with hepatic impairment***
No dose adjustment is necessary *Elderly patients*
No dose adjustment is required for the elderly with normal renal function or creatinine clearance values above 40 ml/min.

***Paediatric population (2-12 years of age) Infections:***
The following table summarizes the treatment frequency and the dose per body weight for paediatric patients 2-12 years of age indication or condition:

| **Dose per weight and treatment frequency** | **Indication / condition** |
|---|---|
| 80 mg Piperacillin / 10 mg Tazobactam per kg body weight / every 6 hours | Neutropenic children with fever suspected to be due to bacterial infections* |
| 100 mg Piperacillin / 12.5 mg Tazobactam per kg body weight / every 8 hours | Complicated intra-abdominal infections* |

* Not to exceed the maximum 4 g / 0.5 g per dose over 30 minutes.

***Patients with renal impairment***
The intravenous dose should be adjusted to the degree of actual renal impairment as follows (each patient must be monitored closely for signs of substance toxicity; medicinal product dose and interval should be adjusted accordingly):

| Creatinine Clearance (ml/min) | Recommended Piperacillin/Tazobactam Dosage |
|---|---|
| > 50 | No dose adjustment needed. |

| | |
|---|---|
| ≤ 50 | 70 mg piperacillin / 8.75 mg tazobactam / kg every 8 hours. |

For children on haemodialysis, one additional dose of 40 mg piperacillin / 5 mg tazobactam / kg should be administered following each dialysis period.

***Use in children aged below 2 years***
The safety and efficacy of piperacillin and tazobactam in children 0- 2 years of age has not been established.

**Treatment duration**
The usual duration of treatment for most indications is in the range of 5-14 days. However, the duration of treatment should be guided by the severity of the infection, the pathogen(s) and the patient's clinical and bacteriological progress.

**Method of administration**
piperacillin and tazobactam 4 g / 0.5 g are administered by intravenous infusion (over 30 minutes). For instructions on reconstitution of the medicinal product before administration.

**4.3 Contraindications**
Hypersensitivity to the active substances, any other penicillin-antibacterial agent. History of acute severe allergic reaction to any other beta-lactam active substances (e.g. cephalosporin, monobactam or carbapenem).

**4.4 Special warnings and precautions for use**
The selection of piperacillin / tazobactam to treat an individual patient should take into account the appropriateness of using a broad-spectrum semi-synthetic penicillin based on factors such as the severity of the infection and the prevalence of resistance to other suitable antibacterial agents.

Before initiating therapy with Piperacillin and Tazobactam, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, other beta-lactam agents (e.g. cephalosporin, monobactam or carbapenem) and other allergens. Serious and occasionally fatal hypersensitivity (anaphylactic/anaphylactoid [including shock]) reactions have been reported in patients receiving therapy with penicillins, including piperacillin / tazobactam. These reactions are more likely to occur in persons with a history of sensitivity to multiple allergens. Serious hypersensitivity reactions require the discontinuation of the antibiotic, and may require administration of epinephrine and other emergency measures.

Piperacillin and tazobactam may cause severe cutaneous adverse reactions, such as Stevens- Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, and acute generalised exanthematous pustulosis. If patients develop a skin rash they should be monitored closely and piperacillin and tazobactam discontinued if lesions progress.

Antibiotic-induced pseudomembranous colitis may be manifested by severe, persistent diarrhoea which may be life threatening. The onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment. In these cases piperacillin and tazobactam, should be discontinued. Therapy with piperacillin and tazobactam may result in the emergence of resistant organisms, which might cause super-infections.

Bleeding manifestations have occurred in some patients receiving beta-lactam antibiotics. These reactions sometimes have 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, the antibiotic should be discontinued and appropriate therapy instituted.

Leukopenia and neutropenia may occur, especially during prolonged therapy; therefore, periodic assessment of haematopoietic function should be performed.
As with treatment with other penicillins, neurological complications in the form of convulsions may occur when high doses are administered, especially in patients with impaired renal function.

Hypokalaemia may occur in patients with low potassium reserves or those receiving concomitant medicinal products that may lower potassium levels; periodic electrolyte determinations may be advisable in such patients.

**Renal Impairment**
Due to its potential nephrotoxicity, piperacillin/tazobactam should be used with care in patients with renal impairment or in hemodialysis patients. Intravenous dosages and administration intervals should be adjusted to the degree of renal function impairment.

In a secondary analysis using data from a large multicenter, randomized-controlled trial when glomerular filtration rate (GFR) was examined after administration of frequently used antibiotics in critically ill patients, the use of piperacillin/tazobactam was associated with a lower rate of reversible GFR improvement compared with the other antibiotics. This secondary analysis concluded that piperacillin/tazobactam was a cause of delayed renal recovery in these patients.

**4.5 Interaction with other medicinal products and other forms of interaction non-depolarising muscle relaxants**
Piperacillin when used concomitantly with vecuronium has been implicated in the prolongation of the neuromuscular blockade of vecuronium. Due to their similar mechanisms of action, it is expected that the neuromuscular blockade produced by any of the non-depolarising muscle relaxants could be prolonged in the presence of piperacillin.

**Oral anticoagulants**

During simultaneous administration of heparin, oral anticoagulants and other substances that may affect the blood coagulation system including thrombocyte function, appropriate coagulation tests should be performed more frequently and monitored regularly.

**Methotrexate**
Piperacillin may reduce the excretion of methotrexate; therefore, serum levels of methotrexate should be monitored in patients to avoid substance toxicity.

**Probenecid**
As with other penicillins, concurrent administration of probenecid and piperacillin / tazobactam produces a longer half-life and lower renal clearance for both piperacillin and tazobactam; however, peak plasma concentrations of either substance are unaffected.

**Aminoglycosides**
Piperacillin, either alone or with tazobactam, did not significantly alter the pharmacokinetics of tobramycin in subjects with normal renal function and with mild or moderate renal impairment. The pharmacokinetics of piperacillin, tazobactam, and the M1 metabolite were also not significantly altered by tobramycin administration.
The inactivation of tobramycin and gentamicin by piperacillin has been demonstrated in patients with severe renal impairment.

**Vancomycin**
No pharmacokinetic interactions have been noted between piperacillin / tazobactam and vancomycin. However, a limited number of retrospective studies have detected an increased incidence of acute kidney injury in patients concomitantly administered piperacillin / tazobactam and vancomycin as compared to vancomycin alone.

**Effects on laboratory tests**
Non-enzymatic methods of measuring urinary glucose may lead to false-positive results, as with other penicillins. Therefore, enzymatic urinary glucose measurement is required under piperacillin and tazobactam therapy. A number of chemical urine protein measurement methods may lead to false-positive results. Protein measurement with dip sticks is not affected.

**4.6 Pregnancy and lactation**
**Pregnancy**
There are no or a limited amount of data from the use of Piperacillin and tazobactam in pregnant women. Piperacillin and tazobactam cross the placenta. Piperacillin / tazobactam should only be used during pregnancy if clearly indicated, i.e. only if the expected benefit outweighs the possible risks to the pregnant woman and foetus.

**Breast-feeding**
Piperacillin is excreted in low concentrations in human milk; tazobactam concentrations in human milk have not been studied. Women who are breast-feeding should be treated only if the expected benefit outweighs the possible risks to the

woman and child.

**4.7 Effects on ability to drive and use machines**
No studies on the effect on the ability to drive and use machines have been performed.

**4.8 Undesirable effects**
The most commonly reported adverse reaction is diarrhoea (occurring in 1 patient out of 10).

Among the most serious adverse reactions pseudo-membranous colitis and toxic epidermal necrolysis occur in 1 to 10 patients in 10,000. The frequencies for pancytopenia, anaphylactic shock and Stevens-Johnson syndrome cannot be estimated from the currently available data.

In the following table, adverse reactions are listed by system organ class and MedDRA-preferred term. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. The following terminologies have been used in order to classify the occurrence of undesirable effects.
Very common (≥1/10) Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)

| Body System | Adverse Reaction |
|---|---|
| *Infections and infestations* | |
| Common: | candida infection |
| *Blood and lymphatic system disorders* | |
| Common: | Thrombocytopenia, anaemia, Coombs direct test positive, activated partial thromboplastin time prolonged. |
| Uncommon | leukopenia, prothrombin time, prolonged |
| Rare: | agranulocytosis, epistaxis |
| Frequency not known (cannot be estimated from available data) | pancytopenia, neutropenia, haemolytic anaemia, purpura, bleeding time prolonged, thrombocytosis, eosinophilia |
| *Immune system disorders* | |
| Frequency not known (cannot be estimated from available data) | Anaphylactoid reaction, anaphylactic reaction, anaphylactoid shock, anaphylactic shock, hypersensitivity |
| *Metabolism and nutritional disorders* | |
| Common | blood albumin decreased; protein total decreased |
| Uncommon | hypokalaemia, blood glucose decreased |
| *Nervous system disorders* | |
| Common | Headache, insomnia |

| | |
|---|---|
| *Vascular disorders* | |
| Uncommon: | Hypotension, phlebitis, thrombophlebitis, flushing |
| *Gastrointestinal disorders* | |
| Very common | Diarrhoea, |
| Common | abdominal pain, vomiting, nausea, constipation, dyspepsia |
| Rare: | Pseudomembranous colitis, stomatitis |
| *Hepatobiliary disorders* | |
| Common | Aspartate aminotransferase increased, alanine aminotransferase increased, blood alkaline phosphatase increased |
| Uncommon | blood bilirubin increased |
| Frequency not known (cannot be estimated from available data) | hepatitis, jaundice, gamma-glutamyl transferase increased |
| *Skin and subcutaneous tissue disorders* | |

| | |
|---|---|
| Common: | rash, pruritus |
| Uncommon: | Erythema multiforme, urticaria, rash maculopapular |
| Rare: | Toxic epidermal necrolysis |
| Frequency not known (cannot be estimated from available data) | Stevens-Johnson syndrome, drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP), dermatitis bullous |
| *Musculoskeletal, connective tissue and bone disorders* | |
| Uncommon | arthralgia, myalgia |
| *Renal and urinary disorders* | |
| Common | blood creatinine increased; blood urea increased |
| Frequency not known (cannot be estimated from available data) | renal failure, tubulointerstitial nephritis |
| *General disorders and administration site conditions* | |
| Common | pyrexia, injection site reaction |
| Uncommon | chills |

Piperacillin therapy has been associated with an increased incidence of fever and rash in cystic fibrosis patients.

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare providers are asked to report any suspected adverse reactions to the marketing authorization holder or if available via the national reporting system (See details below);

*Paper based reporting: TMDA yellow card*
*Online reporting: https://sqrt.tmda.go.tz/*
*USSD reporting: send a simple short text message to report any suspected Adverse Drug Reaction by dialing *152*00# and follow the instructions*.

**4.9 Over dosage Symptoms**

Overdose with piperacillin / tazobactam. The majority of those events experienced, including nausea, vomiting, and diarrhoea, have also been reported with the usual recommended dose.
Patients may experience neuromuscular excitability or convulsions if higher than recommended doses are given intravenously (particularly in the presence of renal failure).

**Treatment**

In the event of an overdose, piperacillin/tazobactam treatment should be discontinued. No specific antidote is known.
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 haemodialysis.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use, Combinations of penicillins incl. beta-lactamase inhibitors;

**Mechanism of action**

Piperacillin, a broad-spectrum, semisynthetic penicillin exerts bactericidal activity by inhibition of both septum and cell wall synthesis.

Tazobactam, a beta-lactam structurally related to penicillins, is an inhibitor of many beta- lactamases, which commonly cause resistance to penicillins and cephalosporins but it does not inhibit AmpC enzymes or metallo beta-lactamases.

Tazobactam extends the antibiotic spectrum of piperacillin to include many beta-lactamase- producing bacteria that have acquired resistance to piperacillin alone.

**Phamacokinetic / Pharmacodynamic relationship**

The time above the minimum inhibitory concentration (T>MIC) is considered to be the major pharmacodynamics determinant of efficacy for piperacillin.

***Mechanism of resistance***

The two main mechanisms of resistance to piperacillin / tazobactam are:

• Inactivation of the piperacillin component by those beta-lactamases that are not inhibited by tazobactam: betalactamases in the Molecular class B, C and D. In addition, tazobactam does not provide protection against extendedspectrum beta-lactamases (ESBLs) in the Molecular class A and D enzyme groups.

• Alteration of penicillin-binding proteins (PBPs), which results in the reduction of the affinity of piperacillin for the molecular target in bacteria.

Additionally, alterations in bacterial membrane permeability, as well as expression of multi-drug efflux pumps, may cause or contribute to bacterial resistance to piperacillin / tazobactam, especially in Gram-negative bacteria.

**Breakpoints**

EUCAST Clinical MIC Breakpoints for Piperacillin / Tazobactam (2009-12-02, v 1). For Susceptibility Testing Purposes, the Concentration of Tazobactam is Fixed at 4 mg/l.

| Pathogen | Species-related breakpoints (S≤/R>) |
|---|---|
| Enterobacteriaceae | 8/16 |

| | |
|---|---|
| Pseudomonas | 16/16 |
| Gram-negative and Gram-positive anaerobes | 8/16 |
| Non-species related breakpoints | 4/16 |

The susceptibility of streptococci is inferred from the penicillin susceptibility. The susceptibility of staphylococci is inferred from the oxacillin susceptibility.

**Susceptibility**

The prevalence of acquired resistance may vary geographically and with time for selected species, and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

| **Groupings of relevant species according to piperacillin / tazobactam susceptibility** |
|---|
| **COMMONLY SUSCEPTIBLE SPECIES** |
| Aerobic Gram-positive micro-organisms<br>*Enterococcus faecalis Listeria monocytogenes*<br>*Staphylococcus aureus,* methicillin-susceptible£<br>*Staphylococcus* species*, coagulase negative*, methicillin-susceptible<br>*Streptococcus pyogenes Group B streptococci* |
| Aerobic Gram-negative micro-organisms<br>*Citrobacter k oseri Haemophilus influenza Moraxella catarrhalis Proteus mirabilis* |
| Anaerobic Gram-positive micro-organisms<br>*Clostridium* species<br>*Eubacterium* species<br>*Peptostreptococcus* species |
| Anaerobic Gram-negative micro-organisms |

| |
|---|
| *Bacteroides fragilis* group *Fusobacterium* species *Porphyromonas* species<br>*Prevotella* species |
| **SPECIES FOR WHICH ACQUIRED RESISTANCE MAY BE A PROBLEM** |
| Aerobic Gram-positive micro-organisms<br>*Enterococcus faecium*$,<br>*Streptococcus pneumonia Streptococcus viridans group* |
| Aerobic Gram-negative micro-organisms<br>*Acinetobacter baumannii*$ *Burk holderia cepacia Citrobacter freundii Enterobacter* species *Escherichia coli Klebsiella pneumonia Morganella morganii Proteus vulgaris Providencia ssp.*<br>*Pseudomonas aeruginosa*<br>*Serratia* species |
| **INHERENTLY RESISTANT ORGANISMS** |
| Aerobic Gram-positive micro-organisms<br>*Corynebacterium jeik eium* |
| Aerobic Gram-negative micro-organisms<br>*Legionella* species<br>*Stenotrophomonas maltophilia* $ |
| Other microorganisms<br>*Chlamydophilia pneumonia Mycoplasma pneumonia* |
| $ Species showing natural intermediate susceptibility. |

£ All methicillin-resistant staphylococci are resistant to piperacillin / tazobactam.

## 5.2 Pharmacokinetic properties

### Absorption
The peak piperacillin and tazobactam concentrations after 4 g / 0.5 g administered over 30 minutes by intravenous infusion are 298 µg/ml and 34 µg/ml respectively.

### 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/tazobactam is widely distributed in tissues and body fluids including intestinal mucosa, gallbladder, lung, bile, and bone. Mean tissue concentrations are generally 50 to 100% of those in plasma. Distribution into cerebrospinal fluid is low in subjects with non-inflamed meninges, as with other penicillins.

### Biotransformation
Piperacillin is metabolised to a minor microbiologically active desethyl metabolite. Tazobactam is metabolised to a single metabolite that has been found to be microbiologically inactive.

### Elimination
Piperacillin and tazobactam are eliminated via the kidney by glomerular filtration and tubular secretion.

Piperacillin is excreted rapidly as unchanged substance, with 68% of the administered dose appearing in the urine. Tazobactam and its metabolite are eliminated primarily by renal excretion, with 80% of the administered dose appearing as unchanged substance and the remainder as the single metabolite. Piperacillin, tazobactam, and desethyl piperacillin are also secreted into the bile.

Following single or multiple doses of piperacillin / tazobactam to healthy subjects, the plasma half- life of piperacillin and tazobactam ranged from 0.7 to 1.2 hours and was unaffected by dose or duration of infusion. The elimination half-lives of both piperacillin and tazobactam are increased with decreasing renal clearance. There are no significant changes in piperacillin pharmacokinetics due to tazobactam. Piperacillin appears to slightly reduce the clearance of tazobactam.

## 6. PHARMACEUTICAL PARTICULARS
### 6.1 List of excipients
None.

### 6.2 Incompatibilities
This medicinal product must not be mixed with other medicinal products. Whenever piperacillin and tazobactam is used concurrently with another antibiotic (e.g.

aminoglycosides), the substances must be administered separately. The mixing of beta-lactam antibiotics with an aminoglycoside *in vitro* can result in substantial inactivation of the aminoglycoside.

Due to chemical instability, piperacillin and tazobactam should not be used in solutions containing only sodium bicarbonate.
Piperacillin and tazobactam should not be added to blood products or albumin hydrolysates.

**Direction for use**
The reconstitution and dilution are to be made under aseptic conditions. The solution is to be inspected visually for particulate matter and discolouration prior to administration. The solution should only be used if the solution is clear and free from particles.

**Intravenous use**
Reconstitute each vial with the volume of solvent shown in the table below, using one of the compatible solvents for reconstitution. Swirl until dissolved. When swirled constantly, reconstitution generally occurs within 5 to 10 minutes (for details on handling, please see below).

| Content of vial | Content of vial |
|---|---|
| 2 g / 0.25 g (2 g piperacillin and 0.25 g tazobactam) | 10 ml |
| 4 g / 0.5 g (4 g piperacillin and 0.5 g tazobactam) | 20 ml |

* Compatible solvents for reconstitution:
- 0.9% (9 mg/ml) sodium chloride solution for injection
- Sterile water for injections$^{\Omega}$
- Glucose 5%

$^{\Omega}$ Maximum recommended volume of sterile water for injection per dose is 50 ml.

The reconstituted solutions should be withdrawn from the vial by syringe. When reconstituted as directed, the vial contents withdrawn by syringe will provide the labeled amount of piperacillin and tazobactam.
The reconstituted solutions may be further diluted to the desired volume (e.g. 50 ml to 150 ml) with one of the following compatible solvents:
- 0.9% (9 mg/ml) sodium chloride solution for injection
- Glucose 5%

**Co-administration with aminoglycosides**
Due to the *in vitro* inactivation of the aminoglycoside by beta-lactam antibiotics, piperacillin and tazobactam and the aminoglycoside are recommended for separate administration. piperacillin and tazobactam and the aminoglycoside should be reconstituted and diluted separately when concomitant therapy with aminoglycosides is indicated. In circumstances where co-administration is recommended, piperacillin and tazobactam is compatible for simultaneous co-administration via Y-site infusion

only with the following aminoglycosides under the following conditions:

| Aminoglycoside | Piperacillin and tazobactam Dose | Piperacillin and tazobactam diluent volume (ml) | Aminoglycoside concentration range* (mg/ml) | Acceptable diluents |
|---|---|---|---|---|
| Amikacin | 2 g / 0.25 g<br>4 g / 0.5 g | 50, 100, 150 | 1.75 – 7.5 | 0.9% sodium chloride or 5% glucose |
| Gentamicin | 2 g / 0.25 g<br>4 g / 0.5 g | 50, 100, 150 | 0.7 – 3.32 | 0.9% sodium chloride or 5% glucose |

* The dose of aminoglycoside should be based on patient weight, status of infection (serious or life-threatening) and renal function (creatinine clearance).

Compatibility of piperacillin and tazobactam with other aminoglycosides has not been established. Only the concentration and diluents for amikacin and gentamicin with the dose of piperacillin and tazobactam listed in the above table have been established as compatible for coadministration via Y-site infusion. Simultaneous co-administration via Y-site in any manner other than listed above may result in inactivation of the aminoglycoside by piperacillin and tazobactam. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

For single use only. Discard any unused solution.

**6.3 Shelf life**
24 months.

**6.4 Special precautions for storage**
Store in a dry place below 30°C.
To reduce the risk of microbial contamination Piperacillin and Tazobactam should be used immediately.
After reconstitution under aseptic conditions, store in a refrigerator at 2-8°C and to be used within 24 hours.

***6.5 Nature and contents of container***
Piperacillin and Tazobactam for Injection 2.25 gm and 4.5 gm*:*
1) A pack of 10 vials, 20 vials, 30 vials & 50 vials.
2) One vial with or without Sterile Water for Injection.

**7. Name of the Marketing Authorisation Holder**
Aurobindo Pharma Ltd, Plot No.: 2, Maitrivihar,
Ameerpet, Hyderabad-500 038, Telangana State,
**India.**

**8. Marketing Authorisation Number(s):**
TAN 20 HM 0524

**9. Date of First Authorisation/Renewal of the Authorisation**
18/11/2020

**10. Date of Revision of the Text**