



Date: 23rd September 2020

To,
The Director,
Ministry of Health (ISP),
Chile.

Subject: Declaration letter for the stability of product Piperacillin and Tazobactam for Injection USP (4.5 gm) 30 ml Glass Vial - Zepita 4.5gm

Respected Sir/Madam,

We, Baxter Pharmaceuticals India Private Limited, would like to register our product Piperacillin and Tazobactam for Injection USP (4.5 gm) 30 ml Glass Vial - Zepita 4.5gm with your esteemed authority ISP, Chile.

We are submitting the stability data of three batches as mentioned in table below in registration dossier. We, hereby declare that Zeiss Pharmaceuticals Pvt. Ltd is the manufacturer of the batches provided in the stability study and also charged and performed the analysis of stability batches.

Stability Condition	Storage Condition	Batch No.	Stability data submitted up to	Stability Study status
Accelerated	40°C ± 2°C & 75%RH ± 5% RH	PIZ16001ZB	6 months	Study Completed
		PIZ16002ZB	6 months	Study Completed
		PIZ16003ZB	6 months	Study Completed
Real time	25°C ± 2°C & 60% RH ± 5% RH	PIZ16001ZB	36 months	Study Completed
		PIZ16002ZB	36 months	Study Completed
		PIZ16003ZB	36 months	Study Completed

Other relevant information are presented in table below:

Details related to	Information
Formulation	<u>Label Claim:</u> Each vial contains: Piperacillin Sodium USP Equivalent to Piperacillin4g Tazobactam Sodium Equivalent to Tazobactam500 mg
Batch manufacturing, analysis and stability site	Zeiss Pharmaceuticals Pvt. Ltd. Plot no.72, EPIP-1 Jharmajri, Baddi, Distt. Solan (H.P.), India.
Name of API supplier used to manufacture stability batches	Aurobindo Pharma Limited, India.
Proposed Shelf Life	24 Months

We request your esteem authority to consider above facts and accept our application.

For, Baxter Pharmaceuticals India Private Limited.

DocuSigned by:
Purohit, Bhranti September 23, 2020
44D781BFE2C84B1...

Authorized Signatory



STANDARD OPERATING PROCEDURE

Zeiss Pharmaceutical Pvt. Ltd, Baddi

Z

Format No. QC/01-028/F02

Version No.: 03

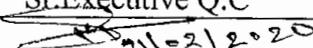
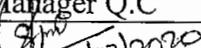
Effective Date:01-04-2010

Page No.: 1 of 2

STABILITY STUDY SUMMARY REPORT (40±2°C, 75±5% RH)

Product Name	Piperacillin & Tazobactam for Injection USP 4.5 gm	Mfg. Date	11/2016
Batch No.	PIZ16001ZB	Exp. Date	10/2018
Storage Condition	40± 2°C; 75±5% RH	Batch Size	22,833 vials
Pack Details	30 ml clear glass vial USP Type-III	Date of Initiation	28/11/2016
Generic Name	Piperacillin & Tazobactam for Injection USP		

Sr. No.	Tests	Specification	Duration (In month)				
			00	01	02	03	06
1.	Description	A white crystalline powder, hygroscopic filled in clear glass vial, sealed with grey coloured butyl rubber stopper, with coloured flip off seal.	Complies	Complies	Complies	Complies	Complies
2.	Identification (By HPLC)	The retention times of the major peaks of the sample solution correspond to those of the standard solution, as obtained in the assay	Complies	Complies	Complies	Complies	Complies
3.	pH(A solution containing the equivalent of 40 mg of Piperacillin per ml)	Between 5.0 to 7.0	5.90	5.96	5.90	5.92	5.93
4.	Water(%w/w) (Use 1.0 g sample)	NMT 2.5 % w/w	1.37%	1.39%	1.43%	1.41%	1.45%
5.	*BET	Not more than 0.08 EU/mg for both	Less than 0.08 EU/mg	NA	NA	NA	Less than 0.08 EU/mg
6.	*Sterility	Should be sterile	Complies	NA	NA	NA	Complies
7.	Particulate matter A)By Visual inspection	The solution should free from foreign particles that can be observed on visual inspection.	Complies	Complies	Complies	Complies	Complies
	*B) By LOPC: ≥10µ ≥25µ	Not more than 6000 Not more than 600	1,774 33	NA NA	NA NA	NA NA	1,057 16

Name	Prepared By Manvendra Singh	Checked By Swatantra Shukla	Approved By Naresh Chauhan
Designation	Sr.Executive Q.C	Asst.Manager Q.C	Sr. Manager Q.C& RA
Sign & Date	 21/02/2020	 22/02/2020	 22/02/2020

STANDARD OPERATING PROCEDURE

Zeiss Pharmaceutical Pvt. Ltd, Baddi

(Z)

Format No. QC/01-028/F02

Version No.: 03

Effective Date:01-04-2010

Page No.: 2 of 2

STABILITY STUDY SUMMARY REPORT (40±2°C, 75±5% RH)

Product Name	Piperacillin & Tazobactam for Injection USP 4.5 gm	Mfg. Date	11/2016
Batch No.	PIZ16001ZB	Exp. Date	10/2018
Storage Condition	40± 2°C; 75±5% RH	Batch Size	22,833 vials
Pack Details	30 ml clear glass vial USP Type-III	Date of Initiation	28/11/2016
Generic Name	Piperacillin & Tazobactam for Injection USP		

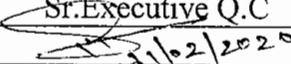
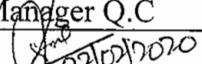
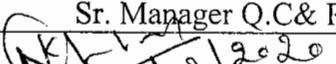
8.	Organic Impurities								
	Tazobactam Related Compound A ^b	NMT 1.0 %		0.027%	0.054%	0.187%	ND	ND	
	Piperacillin Impurity 4 ^c	NMT 1.0 %		0.004%	0.037%	ND	ND	ND	
	Piperacillin penilloic acid ^{d,e}	NMT 1.0 %		0.020%	0.056%	0.054%	0.063%	ND	
	Piperacillin penicilloic acid d ^f	NMT 5.0 %		ND	ND	0.029%	ND	ND	
	Acetylated penicilloic acid of Piperacillin ^g	NMT 1.0 %		ND	0.318 %	ND	ND	ND	
	Piperacillin Impurity 5 ^c	NMT 1.0 %		0.316 %	0.163 %	0.354 %	ND	0.488%	
	Piperacillin Impurity 6 ^c	NMT 1.0 %		ND	ND	0.084%	ND	ND	
	Individual Impurity	NMT 1.0 %		0.082 %	0.144 %	0.051 %	0.090 %	ND	
Total Impurities	NMT 5.0 %		0.571 %	0.799 %	0.732 %	0.351 %	0.488 %		
9.	Assay	Each vial contains :	Limit	Claim					
		Piperacillin Sodium USP g equivalent to Piperacillin	3.600 g to 4.400 g (90.0% to 110.0 %)	4.0	99.8 %	100.6 %	100.9 %	100.7 %	99.2 %
		Each Vials Contains :	Limit	Claim					
		Tazobactam Sodium g equivalent to Tazobactam	0.450 g to 0.550 g (90.0 % to 110.0 %)	0.5 g	98.3 %	100.6%	100.3%	99.9%	97.7%

*To be performed at initial and end of shelf life.

ND-Not Detected

NA-Not Applicable

Remarks: The drug product found to be ~~stable~~ / ~~Unstable~~ at above specified Conditions for period evaluated of06thmonth's data & Completed at 06th month.

	Prepared By	Checked By	Approved By
Name	Manvendra Singh	Swatantra, Shukla	Naresh Chauhan
Designation	Sr. Executive Q.C	Asst. Manager Q.C	Sr. Manager Q.C & RA
Sign & Date	 21/02/2020	 22/02/2020	 22/02/2020

STANDARD OPERATING PROCEDURE

Zeiss Pharmaceutical Pvt. Ltd, Baddi

②

Format No. QC/01-028/F02

Version No.: 03

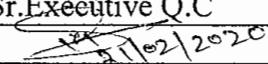
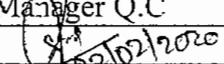
Effective Date:01-04-2010

Page No.: 1 of 2

STABILITY STUDY SUMMARY REPORT (25-2°C, 60±5% RH)

Product Name	Piperacillin & Tazobactam for Injection USP 4.5 gm	Mfg. Date	11/2016
Batch No.	PIZ16001ZB	Exp. Date	10/2018
Storage Condition	25± 2°C; 60±5% RH	Batch Size	22,833 vials
Pack Details	30 ml clear glass vial USP Type-III	Date of Initiation	28/11/2016
Generic Name	Piperacillin & Tazobactam for Injection USP		

Sr. No.	Tests	Specification	Duration (In month)							
			00	03	06	09	12	18	24	36
1.	Description	A white crystalline powder, hygroscopic filled in clear glass vial, sealed with grey coloured butyl rubber stopper, with coloured flip off seal.	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies
2.	Identification (By HPLC)	The retention times of the major peaks of the sample solution correspond to those of the standard solution ,as obtained in the assay	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies
3.	pH(A solution containing the equivalent of 40 mg of Piperacillin per ml)	Between 5.0 to 7.0	5.90	5.88	5.36	5.91	6.08	6.01	5.86	5.91
4.	Water(%w/w) (Use 1.0 g sample)	NMT 2.5 % w/w	1.37%	1.39%	1.44%	1.47%	1.58%	1.31%	1.40%	1.40%
5.	*BET	Not more than 0.08 EU/mg for both	Less than 0.08 EU/mg	NA	NA	NA	NA	NA	NA	Less than 0.08 EU/mg
6.	*Sterility	Should be sterile	Complies	NA	NA	NA	NA	NA	NA	Complies
7.	Particulate matter A)By Visual inspection	The solution should free from foreign particles that can be observed on visual inspection.	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies

	Prepared By	Checked By	Approved By
Name	Manvendra Singh	Swatantra Shukla	Naresh Chauhan
Designation	Sr.Executive Q.C	Asst.Manager Q.C	Sr. Manager Q.C& RA
Sign & Date	 27/02/2020	 28/02/2020	 28/02/2020

STANDARD OPERATING PROCEDURE

Zeiss Pharmaceutical Pvt. Ltd, Baddi

Z

Format No. QC/01-028/F02

Version No.: 03

Effective Date:01-04-2010

Page No.: 2 of 2

STABILITY STUDY SUMMARY REPORT (25±2°C, 60±5% RH)

Product Name	Piperacillin & Tazobactam for Injection USP 4.5 gm	Mfg. Date	11/2016
Batch No.	PIZI6001ZB	Exp. Date	10/2018
Storage Condition	25± 2°C; 60±5% RH	Batch Size	22,833 vials
Pack Details	30 ml clear glass vial USP Type-III	Date of Initiation	28/11/2016
Generic Name	Piperacillin & Tazobactam for Injection USP		

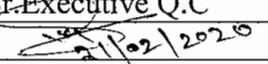
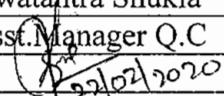
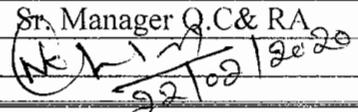
	*B) By LOPC: $\geq 10\mu$ $\geq 25\mu$	Not more than 6000 Not more than 600	1,774 33	NA NA	NA NA	NA NA	NA NA	NA NA	NA NA	4.483 255
8.	Organic Impurities									
	Tazobactam Related Compound A ^b	NMT 1.0 %	0.027%	ND						
	Piperacillin Impurity 4 ^c	NMT 1.0 %	0.004%	ND						
	Piperacillin penilloic acid ^{d,e}	NMT 1.0 %	0.020%	0.113%	ND	ND	ND	ND	ND	ND
	Piperacillin penicilloic acid d ^f	NMT 5.0 %	ND	ND	ND	ND	ND	ND	ND	ND
	Acetylated penicilloic acid of Piperacillin ^g	NMT 1.0 %	ND	ND	ND	0.092%	ND	ND	ND	ND
	Piperacillin Impurity 5 ^c	NMT 1.0 %	0.316 %	0.431 %	0.335 %	ND	ND	ND	ND	ND
	Piperacillin Impurity 6 ^c	NMT 1.0 %	ND	ND	ND	ND	ND	ND	ND	ND
	Individual Impurity	NMT 1.0 %	0.082 %	0.199 %	ND	0.437%	0.374%	0.318%	0.530%	0.370%
	Total Impurities	NMT 5.0 %	0.571 %	0.872 %	0.335 %	0.825 %	0.669 %	0.636 %	0.599 %	0.810 %
9.	Assay	Each vial contains : Limit Claim Piperacillin Sodium USP 3.600 g to 4.400 g 4.0 g equivalent to Piperacillin (90.0% to 110.0 %)	99.8 %	100.0 %	100.0 %	99.8 %	99.6 %	99.3 %	99.8 %	99.2 %
		Each Vials Contains : Limit Claim Tazobactam Sodium 0.450 g to 0.550 g 0.5 g equivalent to Tazobactam (90.0 % to 110.0 %)	98.3 %	98.3 %	97.9 %	98.9 %	98.4 %	100.0 %	98.8 %	98.5 %

*To be performed at initial and end of shelf life.

ND-Not Detected

NA-Not Applicable

Remarks: The drug product found to be ~~stable~~ / ~~Unstable~~ at above specified Conditions for period evaluated of36thmonth's data & Completed at 36th month.

	Prepared By	Checked By	Approved By
Name	Manvendra Singh	Swatantra Shukla	Naresh Chauhan
Designation	Sr.Executive Q.C	Asst.Manager Q.C	Sr. Manager Q.C& RA
Sign & Date	 21/02/2020	 22/02/2020	 22/02/2020

STANDARD OPERATING PROCEDURE

Zeiss Pharmaceutical Pvt. Ltd, Baddi

(Z)

Format No. QC/01-028/F02

Version No.: 03

Effective Date:01-04-2010

Page No.: 2 of 2

STABILITY STUDY SUMMARY REPORT (25±2°C, 60±5% RH)

Product Name	Piperacillin & Tazobactam for Injection USP 4.5 gm	Mfg. Date	11/2016
Batch No.	PIZ16003ZB	Exp. Date	10/2018
Storage Condition	25± 2°C; 60±5% RH	Batch Size	20,758 vials
Pack Details	30 ml clear glass vial USP Type-III	Date of Initiation	28/11/2016
Generic Name	Piperacillin & Tazobactam for Injection USP		

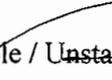
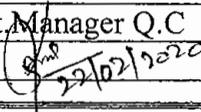
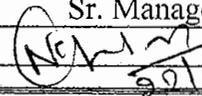
	*B) By LOPC: ≥10µ ≥25µ	Not more than 6000 Not more than 600	1,641 41	NA NA	NA NA	NA NA	NA NA	NA NA	NA NA	2,125 86
8.	Organic Impurities Tazobactam Related Compound A ^b Piperacillin Impurity 4 ^c Piperacillin penilloic acid ^{d,e} Piperacillin penicilloic acid d ^f Acetylated penicilloic acid of Piperacillin ^g Piperacillin Impurity 5 ^c Piperacillin Impurity 6 ^c Individual Impurity Total Impurities	NMT 1.0 % NMT 1.0 % NMT 1.0 % NMT 5.0 % NMT 1.0 % NMT 1.0 % NMT 1.0 % NMT 1.0 % NMT 5.0 %	 0.024% 0.023% 0.013% 0.008% 0.337 % 0.009 % ND 0.072 % 0.571 %	 ND ND 0.088% ND ND ND ND ND 0.123 % 0.453 %	 ND ND ND ND ND 0.441% ND 0.050 % 0.492 %	 ND ND ND ND 0.67% ND ND 0.399 % 0.667 %	 ND ND ND ND ND ND ND ND 0.503 % 0.930 %	 ND ND ND ND ND ND ND ND 0.403 % 0.762 %	 ND ND ND ND ND ND ND ND 0.503 % 0.503 %	 ND ND ND ND ND ND ND ND 0.400 % 0.610 %
9.	Assay	Each vial contains : Limit Claim Piperacillin Sodium USP 3.600 g to 4.400 g 4.0 g equivalent to Piperacillin (90.0% to 110.0 %) Each Vials Contains : Limit Claim Tazobactam Sodium 0.450 g to 0.550 g 0.5 g equivalent to Tazobactam (90.0 % to 110.0 %)	99.7 % 98.2 %	100.6 % 98.0 %	99.1 % 98.8 %	101.3 % 97.9 %	101.1 % 97.9 %	98.9 % 97.7 %	98.6 % 97.6 %	98.4 % 97.9 %

*To be performed at initial and end of shelf life.

ND-Not Detected

NA-Not Applicable

Remarks: The drug product found to be stable / ~~unstable~~ at above specified Conditions for period evaluated of36thmonth's data & Completed at 36th month.

	Prepared By	Checked By	Approved By
Name	Manvendra Singh	Swatantra Shukla	Naresh Chauhan
Designation	Sr.Executive Q.C	Asst.Manager Q.C	Sr. Manager Q.C& RA
Sign & Date	 21/02/2020	 22/02/2020	 20/02/2020

	Zeiss Pharmaceuticals Pvt. Ltd, Baddi (H.P.)		Page No.	1 of 10	
	RECONSTITUTION STABILITY DATA OF PIPERACILLIN & TAZOBACTAM 4.5 G				
	DEPARTMENT : QUALITY CONTROL				
Product Name :	Piperacillin & Tazobactam for Injection USP 4.5 g	Protocol No:	QUAL/ST/REC/15-00		
Specification No:	FSP/151U-01				

**RECONSTITUTION STABILITY DATA
WITH
STERILE WATER FOR INJECTION**

Protocol No.	QUAL/ST/REC/15-00
Total No. of Pages	10

Zeiss Pharmaceuticals Pvt. Ltd.
72, Export Promotion Industrial Park,
Phase-I, Jharmajri, Baddi,
Himachal Pradesh, India



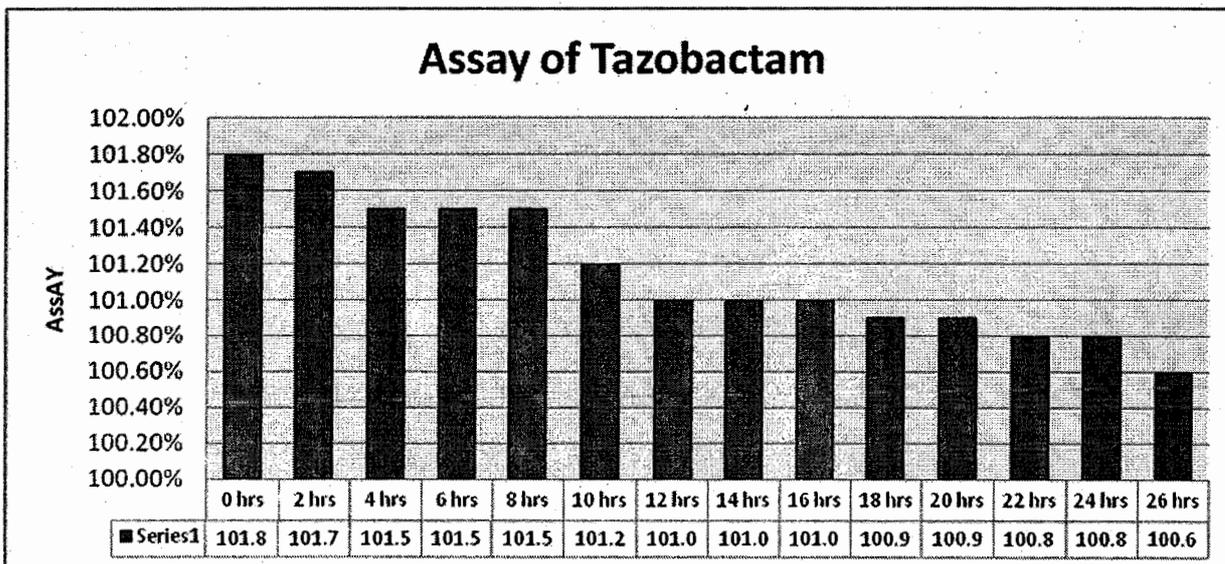
Zeiss Pharmaceuticals Pvt. Ltd,
Baddi (H.P.)

Page No. 10 of 10

RECONSTITUTION STABILITY DATA OF
PIPERACILLIN & TAZOBACTAM 4.5 G
DEPARTMENT : QUALITY CONTROL

Product Name :	Piperacillin & Tazobactam for Injection USP 4.5 g	Protocol No:	QUAL/ST/REC/15-00
Specification No:	FSP/151U-01		

Assay of Tazobactam



8.0 CONCLUSION:

Based on above study we concluded that the reconstitution stability with Sterile water for Injection. Piperacillin & Tazobactam for Injection 4.5 g is stable for 24 hrs at pH, Assay and Colour of reconstituted solution.
All the results are within acceptance criteria.

Prepared By
Sign/Date
[Signature]
23-02-2015

Checked By
Sign/Date
[Signature]
23-02-2015

Approved By
Sign/Date
[Signature]
23/02/15