PROCESS VALIDATION PROTOCOL

Generic Name	**RAMITHIAZIDE 5/12.5**
Label claim	Each Uncoated tablet contains: Ramipril BP.....5 mg Hydrochlorothiazide BP.....12.5 mg Excipients.....q.s. Colour: Erythrosine Supra
Dosage Form	Tablets
Reference BMR No	BMR/T/134-00
Batch Size	600000
Shelf Life	36Months
MFG. LIC. NO.	**PON/DRUGS/19 13 4323**

PROTOCOL APPROVAL

	Department	Name	Designation	Sign & date
Prepared by	Quality Assurance	RAMKUMAR	Executive	23/10/2020
Reviewed by	Production	P. ARULKRISHNAN	Asst. Manager	P. Arul 23/10/2020
	Quality Control	A. VALLARASU	Manager	23/10/2020
Approved by	Quality Assurance	R. STEPHEN.	Dy. MANAGER	23/10/2020

1.0 TABLE OF CONTENTS

Generic name	RAMITHIAZIDE 5/12.5	Effective Date	24/10/2020
Protocol No.	PVP-R09	Ref. SOP No.	QAGN/017

2.0 OBJECTIVE

To monitor the process for establishing documented evidence to ensure that the process variables including the critical process parameters are under control and to demonstrate that the process consistently produces a product meeting its predetermined specification and quality attributes.

3.0 SCOPE

The validation activity shall be carried out to ensure that this product, meets predetermined specification and quality attributes when manufactured in stages from Dispensing, Granulation, Compression and Packing.

4.0 RESPONSIBILITY

Department	Responsibilities
Quality Assurance	To prepare, review, approved and authorized the protocol. Execution these protocol samplings during validation as per sampling plan.
Production	To review and approve the protocol and to co-ordinate and support for process validation.
Quality Control	To review and approve the protocol and responsible to analysis of collected samples.

5.0 IDENTIFICATION OF VALIDATION TEAM AND TRAINING

Personnel shall be identified from QA, QC, PD department and trained for executing this validation activity.

S. No.	Name	Department	Designation	Sign/Date
01	RAMKUMAR	QA	Executive	
02	S. Anbarasan	QA	Trainee	
03	Santhiya	Packing	Chemist	
04	N. Balabasker	Production	Trainee chemist	N. Bal
05	M. Sadishkumar	Stores	Executive	M. Sad
06	C. Prabahakaran	QA	Trainee	

Training details

Name of the trainer: Stephen - R

Duration: 45 min

Signature Of trainer:

Training details shall be attached in training attendance sheet.

Generic name	RAMITHIAZIDE 5/12.5	Effective Date	24/10/2025
Protocol No.	PVP-R09	Ref. SOP No.	QAGN/017

6.0 ABBREVIATIONS

Acronym	Definition	Acronym	Definition
P	Protocol	NMT	Not more than
QA	Quality Assurance	°C	Degree Celsius
QC	Quality Control	%	Percentage
PV	Process validation	mg.	Milligram
BMR	Batch manufacturing record	RPM	Rotation per minute
TABS	Tablets	RSD	Relative standard deviation
IP	Indian pharmacopeia	OOS	Out of Specification
BP	British pharmacopeia	g.	Gram
USP	United states pharmacopeia	Kg.	Kilogram
ICH	International conference on harmonization	lt.	Litre
cGMP	Current Good Manufacturing practices	mm.	Millimetre
IH	In house	ml.	Millilitre
API	Active pharmaceutical ingredient	NLT	Not less then
PD	Production	FG	Finished goods
ID	Identification	RH	Relative humidity
S.	Serial	R-LAF	Reverse laminar Air flow
No.	Number	LOD	Loss on drying
CPP	Critical process parameter	DT	Disintegration time
CQA	Critical quality attributes	Qty.	Quantity
CPC	Critical process control	IPC	In process container
UV	Ultra violet	NA	Not applicable
HPLC	High performance liquid chromatography	MLT	Microbial limit test
Max.	Maximum	HMI	Human Machine Interface
Min.	Minimum		

7.0 TYPE OF VALIDATION

Prospective validation	-
Concurrent validation	√
Re-validation	-

Generic name	RAMITHIAZIDE 5/12.5	Effective Date	24/10/2020
Protocol No.	PVP-R09	Ref. SOP No.	QAGN/017

8.0 REASON FOR VALIDATION

Reasons	Tick in the appropriate row	Reasons	Tick in the appropriate row
New formulation	-	Significant changes in process	-
Change in formulation	-	Change/modification in equipment	-
Change in location	√	Any other reasons (specify)	Concurrent validation
Critical change in some of materials	-		

9.0 PRE REQUISITES OF PROCESS VALIDATION

1. The batches will be manufactured as per the respective batch manufacturing record.
2. The equipments utilized for manufacturing as per list of equipments and BMR.
3. The raw material used for manufacturing will be from approved manufacturer and shall be released by quality control.
4. The critical process parameters of the process will be evaluated with respect to quality attributes of the products
5. Sampling of in-process samples will be carried as per established sampling procedure and plan.
6. Critical in-process will be evaluated with respect to the laid down specification.
7. Finished drug product of these batches will be analysed as per laid down test procedures and comply with respect to the specifications.

10.0 PRODUCT DETAILS

Product Name	RAMITHIAZIDE 5/12.5		
Dosage Form	Oral Tablet		
Label Claim	Each Uncoated tablet contains: Ramipril BP.....5 mg Hydrochlorothiazide BP.....12.5 mg Excipients.....q.s. Colour: Erythrosine Supra		
Average weight of Coated tablet	200.00 mg		
Batch number	1	2	3
	GF201004	GF201207	GF210314
Batch size	6.0L	6.0L	6.0L
Manufacturing date	10/2020	12/2020	03/2021
Expiry date	09/2023	11/2023	02/2024
Started on	26/10/2020	24/12/2020	31/03/2021
Completed on	07/11/2020	05/01/2021	24/04/2021

11.0 BILL OF MATERIALS

Sr. No.	Name of the Ingredient	Spec.	Item Code	Quantity/ Tablets (mg)	Std. quantity per 6,00,000 tablets (kg)	OA/ PL (%)	Req. quantity per 6,00,000 tablets (kg)
Dry mixing material:							
1	Ramipril*	BP	RAI/SP/R006	5.000	3.000	2	3.060
2	Hydrochlorothiazide^	BP	RAI/SP/H001	12.500	7.500	2	7.650
3	Maize Starch**^^	BP	REX/SP/M013	61.400	36.840	-	36.840
4	Lactose Monohydrate	IP	REX/SP/L003	74.000	44.400	-	44.400
5	Microcrystalline Cellulose PH 102	IP	REX/SP/M014	30.000	18.000	-	18.000
Binder Material:							
6	Gelatin	IP	REX/SP/G001	2.000	1.200	-	1.200
7	Maize Starch	BP	REX/SP/M013	5.000	3.000	-	3.000
8	Erythrosine Supra	IHS	REX/SP/E005	0.100	0.060	-	0.060
9	Purified Water	BP	NA	q.s.	30.000	-	30.000
	Theoretical Weight of Dried Granules			**190.000**	**114.000**	-	**114.210**
Lubrication Material:							
10	Sodium Starch Glycollate	BP	REX/SP/S004	5.000	3.000	-	3.000
11	Colloidal Silicon Dioxide	BP	REX/SP/C001	1.000	0.600	-	0.600
12	Magnesium Stearate	IP	REX/SP/M011	4.000	2.400	-	2.400
	Theoretical Weight of the Lubricated granules			**200.000**	**120.000**	-	**120.210**
	Theoretical weight of Compressed tablet			**200.000**	**120.000**	-	**120.210**

Generic name	RAMITHIAZIDE 5/12.5	Effective Date	24/10/2020
Protocol No.	PVP-R09	Ref. SOP No.	QAGN/017

12.0 RAW MATERIALS MANUFACTURER - API

1.0 RAMIPRIL: **Manufacturer Name:** _____

A.R. No	Batch No	Mfg. date	Exp. date	Qty.

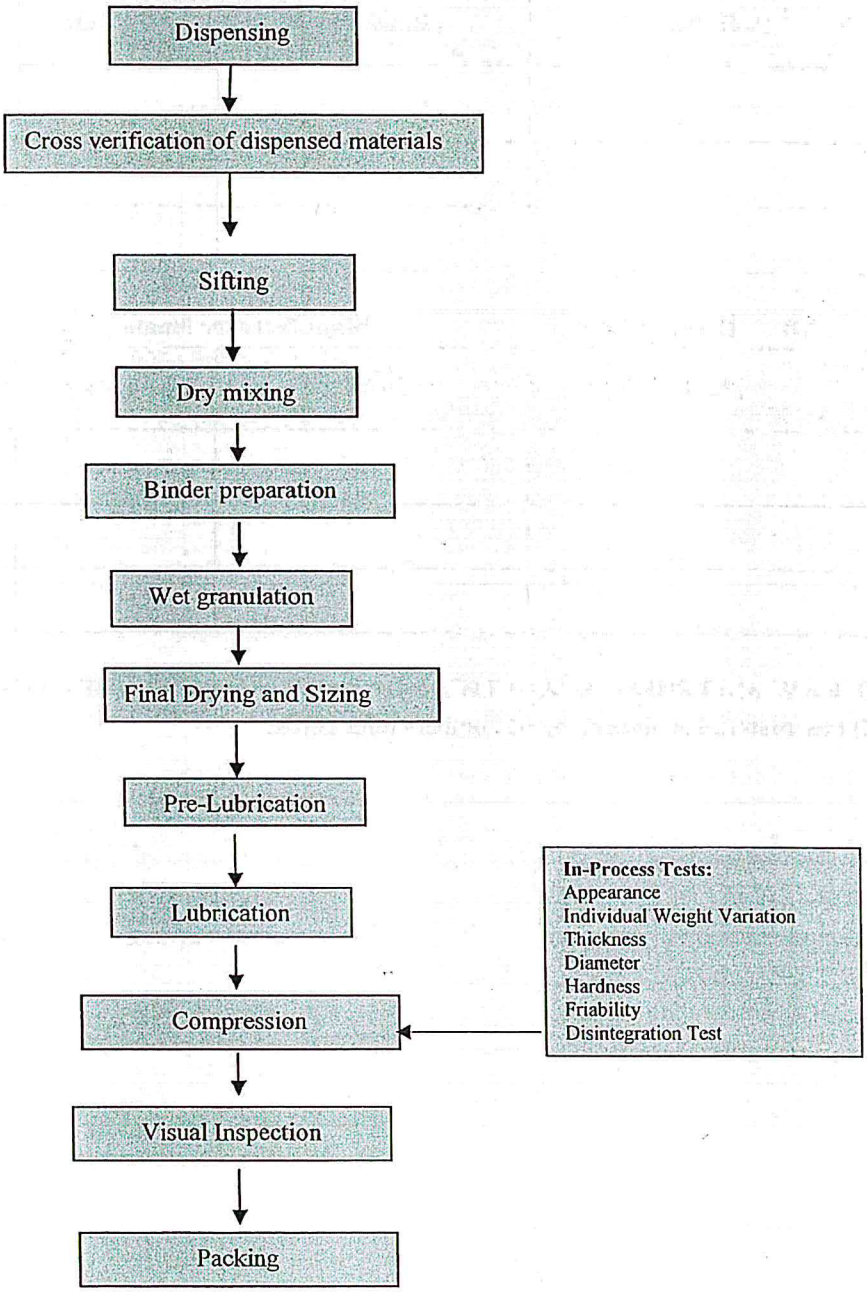
2.0 RAMIPRIL: **Manufacturer Name:** _____

A.R. No	Batch No	Mfg. date	Exp. date	Qty.

13.0 RAW MATERIAL ANALYTICAL REPORT NUMBERS USED FOR BATCHES

All raw material analytical report numbers refer BMR.

14.0 PROCESS FLOWCHART



Generic name	RAMITHIAZIDE 5/12.5	Effective Date	24/10/2020
Protocol No.	PVP-R09	Ref. SOP No.	QAGN/017

15.0 CRITICAL PROCESS PARAMETERS AND CRITICAL PROCESS ATTRIBUTES

S. No	Process stage	CPP	CQA	CPC	Rational for selection	Process verification
1.	Dispensing	Weighing balance	Weight variation	Manual	Critical process leads to affect product quality	Monthly calibration status and daily verification status will be verified before the use.
2.	Vibratory sifter	Sieve size	Size reduction	Manual	Size of the partial may leads to product quality	Sieve size selection done based on BMR. Sieve integrity shall be verified before and after use.
3.	Dry Mixing	Mixing Time and Speed	Uniformity	Auto/ manual	RPM and mixing time will affect the affect product quality	Mixing time and speed shall be concluded after execution of batches.
4.	Drying	Inlet, bed temperature and Drying Time	Loss on drying	Auto/ manual	LOD will affect the affect product quality	Sampling locations shall be identified based on the occupancy of Drier.
5.	Size reduction	Screen size	Size reduction	Manual	Size of the partial may leads to product quality	Screen size selection done based on BMR.
6.	Blending	RPM & Time	Assay and blend uniformity.	Manual	RPM and mixing time will affect the affect product quality.	• Set RPM & time intervals samples shall be collected. • Sampling locations shall be identified based on the occupancy of blender. • Blending/ lubrication time shall be concluded after execution of batches.
7.	Compression	Turret RPM Compression pressure Hopper level	Physical, chemical properties of tablets.	Manual	Turret speed, pressure, granule level in hopper will affect product quality.	• Sample shall be collect at thickness, various speed, hopper level • Turret RPM & pressure shall be verified.
8.	Packing	Machine speed	Description of tablets, leak test.	Manual	• Forming and sealing quality • Speed of the machine	Check the forming temperature, sealing temperature and machine speed, Leak test.

16.0 STAGE WISE SAMPLING LOCATION AND SAMPLE QUANTITY

Stage	Sample Location	Sample size		Test
At Dry Mixing stage (withdraw sample at 9, 10 and 11Min)	10Location Sample and Composite	Unit dose 1x to 3x, where x = 182.9 **mg (182.9 mg to 548.7 mg).**		Blend uniformity and Assay
At Lubrication stage(withdraw sample at 2, 3 and 4Mins)	10Location Sample	Unit dose 1x to 3x, where x = 150 **mg (200 mg to 600 mg).**		Blend uniformity
Lubricated Blend	Composite sample	75 gm		Complete analysis as per in-process lubricated granules specification
Compression	Hardness Challenge	LHS RHS	50 tablets	Description, average weight, Uniformity of weight, thickness, hardness, friability, disintegration time and Dissolution.
Compression	Speed challenge (RPM)	LHS RHS	50 tablets	Description, average weight, Uniformity of weight, thickness, hardness, friability, disintegration time and Assay
Compression	Hopper level challenge	LHS RHS	75 tablets	Description, average weight, Uniformity of weight, thickness, hardness, friability, disintegration time and Content Uniformity
Compression	Composite sample	100 tablets		Description, average weight, Uniformity of weight, thickness, hardness, friability, disintegration time and Assay
Finished Product	120tabs			Complete analysis as per in-process compressed tablets specification Microbial tests as per finished product specification
Packing (withdraw sample at High Temp & Low RPM)	temperature challenge Speed challenge.	10 blisters or entire sealing drum		Appearance, Leak test and Assay

17.0 ACCEPTANCE CRITERIA FOR ALL STAGES

17.1 In process specification for Dry Mixing:

S. No.	Test	Specification
1.	Appearance	white colour granular powder
2.	Blend uniformity (Ramipril BP and Hydrochlorothiazide BP)	NLT 90% and NMT 110.0%
3.	Assay (Ramipril BP and Hydrochlorothiazide BP)	NLT 90% and NMT 110.0%

17.2 In process specification for Dry Mixing:

S. No.	Test	Specification
1.	Appearance	Pink colour granular powder
2.	Blend uniformity (Ramipril)	NLT 90% and NMT 110.0%
3.	%RSD	NMT 5 %
4.	Bulk density	For information only
5.	Tap density	For information only
6.	Particle size	For information only
7.	LOD	For information only
8.	Assay (Ramipril)	NLT 90% and NMT 110.0%

17.3 In process product specification (Core Tablets Specification)

S. No.	Test	Specification
1.	Description	Pink coloured, circular shaped, uncoated tablet with breakline on one side and plain on other side
2.	Identification by IR	The infrared absorption spectrum of the residue is concordant with the reference spectrum of Ramipril & Hydrochlorthiazide
3.	Group Weight	4.000 g± 3.0 % (3.880 gm to 4.120 gm)
4.	Average Weight of Tablets	200.000 mg ± 3.0 % (194.000 mg – 206.000 mg)
5.	Uniformity of weight Tablets	Not More Than 2 of the Individual weights deviate from the average by more than ± 7.5% and more deviate by more than ± 15.0%
6.	Diameter	7.93 mm ± 0.2mm
7.	Hardness	NLT 3.0 Kg
8.	Thickness (mm)	3.20 mm ±0.3 (2.90 mm - 3.50 mm)
9.	Friability	NMT 1 % w/w
10.	Disintegration Time	NMT 15 Minutes
11.	Assay Each Uncoated Tablet Contains:	NLT 90.0% NMT 110.0%
12.	Content Uniformity	NLT 85.0% and NMT 115.0%
13.	Dissolution:	NLT 85.0% of the label claim

14.	**Related Substance**	Impurity A NMT 2.0% Impurity D NMT 6.0% Impurity E NMT 2.0% Single Maximum unknown impurity NMT0.5% Total Impurities NMT 6.0%
15.	**Microbiological Limits** Total Aerobic Microbial counts Fungi E.coli Salmonella S.Aureus P. aeruginosa	 NMT 1000 cfu/g NMT 100 cfu/g Should Be absent Should Be absent Should Be absent Should Be absent

18.0 PRODUCT ASSESSMENT CRITERIA

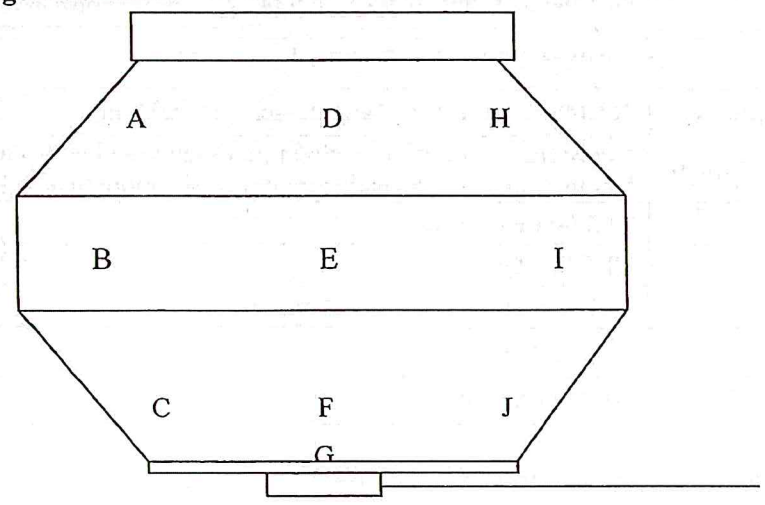
The data will be collected, summarized and a conclusion will be drawn. Any out of specification/Deviation should be investigated. The results should meet limits of acceptance specifications.

19.0 NON COMPLIANCE

Details of deviation (including justification of acceptance if any) done to successfully carryout the validation exercise and any OOS results obtained should be recorded.

20.0 SAMPLING LOCATIONS DIAGRAMS.

1. **Octagonal blender:**



SYMBOL	Location	SAMPLING LOCATION DETAILS
A	Left- Top	From the left side corner near wall side of the blender approx. 2 inch below the top surface of the powder bed.
B	Left- Middle	From the left middle corner near wall side of the blender approx. 5 inch below the top surface of the powder bed.
C	Left- Bottom	From the left side bottom wall side of the blender approx. 2 inch away from the left side of the wall.
D	Center- Top	From the center of the blender approx. 2 inch below the top surface of the powder bed.
E	Center-Middle	From the center of the blender middle surface of the powder bed.
F	Center-Bottom	From the center bottom of the blender bottom layer of the powder bed.
G	Discharge-Port	Approx. center of the discharge port of the blender.
H	Right-Middle	From the right middle corner near side of the blender approx. 2 inch below the top surface of the powder bed.
I	Right-Bottom	From the right-side bottom wall of the blender approx. 2 inch away from the right side of wall.
J	Right-Top	From the right side, corner near wall of the blender approx. 2 inch below the top surface of the powder bed.
Composite Sample		Composite sample from all location.

21.0 REFERENCE DOCUMENTS

To prepare the validation protocol current version of below mentioned documents are referred, which provide Adequate information of manufacturing & packing process.

Sl No	Documents	Ref. No.
1	Master Formula Record (MFR)	MFR/T/058-00
2	Batch Manufacturing Record (BMR)	BMR/T/134-00
3	Batch Packing Record (BPR)	BPR/T/134-00
4	Finished Product Specification (FPS)	FPS: R09
5	Process Validation SOP	QAGN/017

22.0 REVISION HISTORY

S. No.	Effective date	Version No.	Reason for changes
01	24/10/2020.	00	New document

23.0 ATTACHMENTS

Analytical reports shall be attached in process validation report.

24.0 REPORT

After execution of protocol, report will be prepared and final conclusion will be drawn.

PROCESS VALIDATION REPORT

Generic Name	**RAMITHIAZIDE 5/12.5**
Label claim	**Each Uncoated tablet contains:** Ramipril BP.....5 mg Hydrochlorothiazide BP.....12.5 mg Excipients.....q.s. Colour: Erythrosine Supra
Dosage Form	Tablets
BMR No	BMR/T/134-00
Batch Size	600000
Shelf Life	36 Months
MFG. LIC. NO.	PON/DRUGS/19 13 4323
Product Code	**R09**

1.0 TABLE OF CONTENT

2.0 OBJECTIVE

To ensure that the critical process variables are checked during validation and to demonstrate the process capability on equipment and utility ensuring that the product meets it predetermined specifications and quality attributes.

The Process validation is being taken for generation of sufficient data and establishing of standard manufacturing process. Three consecutive batches of **RAMITHIAZIDE 5/12.5** have taken up for Process Validation. If any problem is observed during manufacturing, the Process Validation shall be extended to other three consecutive batches.

3.0 SCOPE

The scope of this report is limited to the Process Validation of **RAMITHIAZIDE 5/12.5**, which defines the procedural aspects to be followed while carrying out process validation activity that includes prerequisites before commencing the actual work.

This report is applicable for the process validation of **RAMITHIAZIDE 5/12.5** to be manufactured at : Generic Health Care Private Limited , Puducherry.

4.0 RESPONSIBILITY

The validation group, comprising of a representative from each of the following departments, shall be responsible for the overall compliance of this report:

Functional Area	Responsibility
Production	• Execution of Process Validation Batch. • Review of Process Validation Report.
Quality Assurance	• Co-ordination with Production and QC to carryout process validation batch. • Monitoring and sampling at the different stages. • Checking and approval of Process Validation Report.
Quality Control	• Analysis of validation batch samples. • Preparation of analytical report and submit to Quality Assurance Department. • Review of Process Validation Report.
Maintenance	• To provide necessary utility and environmental condition in process equipment and area

5.0 ABBREVIATIONS

Acronym	Definition		Acronym	Definition
P	Protocol		NMT	Not more than
QA	Quality Assurance		°C	Degree Celsius
QC	Quality Control		%	Percentage
PV	Process validation		mg.	Milligram
BMR	Batch manufacturing record		RPM	Rotation per minute
TABS	Tablets		RSD	Relative standard deviation
IP	Indian pharmacopeia		OOS	Out of Specification
BP	British pharmacopeia		g.	Gram
USP	United states pharmacopeia		Kg.	Kilogram
ICH	International conference on harmonization		lt.	Litre
cGMP	Current Good Manufacturing practices		mm.	Millimeter
IH	In house		ml.	Milliliter
API	Active pharmaceutical ingredient		NLT	Not less then
PD	Production		FG	Finished goods
ID	Identification		RH	Relative humidity
S.	Serial		R-LAF	Reverse laminar Air flow
No.	Number		LOD	Loss on drying
CPP	Critical process parameter		DT	Disintegration time
CQA	Critical quality attributes		Qty.	Quantity
CPC	Critical process control		IPC	In process container
UV	Ultra violet		NA	Not applicable
HPLC	High performance liquid chromatography		MLT	Microbial limit test
Max.	Maximum		HMI	Human Machine Interface
Min.	Minimum			

Generic name	**RAMITHIAZIDE 5/12.5**
Protocol No.	**PVR-R09**

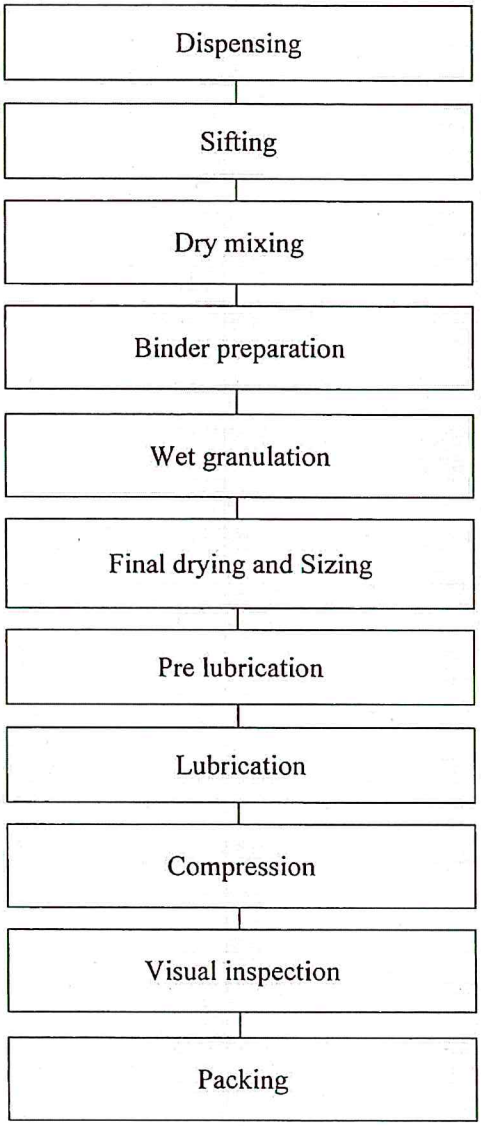
6.0 PRODUCT DETAILS

Generic Name	**RAMITHIAZIDE 5/12.5**		
Dosage Form	Oral Tablet		
Label Claim	Each Uncoated tablet contains: Ramipril BP.....5 mg Hydrochlorothiazide BP.....12.5 mg Excipients.....q.s. Colour: Erythrosine Supra		
Average weight of coated tablet	200.00mg		
Batch number	GF201004	GF201207	GF210317
Batch size	**6.0L**	**6.0L**	**6.0L**
Manufacturing date	10/2020	12/2020	03/2021
Expiry date	09/2023	11/2023	02/2024
Started on	26/10/2020	24/12/2020	31/03/2021
Completed on	07/11/2020	05/01/2021	27/04/2021

7.0 PROCESS EQUIPMENT DESCRIPTION

S. No.	Equipment name	Equipment ID No	Calibration/qualification status Next calibration due
1.	Dispensing Booth	ST/DPB/001	Qualified
2.	Vibratory sifter	PDVBS/001	Qualified
3.	Octagonal blender	PD/OCB/001	Qualified
4.	Compression machine	PD/COM/002	Qualified
5.	Packing machine (Alu Alu Packing)	PD/ALU/001	Qualified
6.	Weighing balance (IPQA)	QA/BAL/002	Calibrated
7.	Vernier caliper	QAVEC/001	Calibrated
8.	Friability apparatus	QA/FRT/001	Calibrated
9.	Hardness tester	QA/HRD/001	Calibrated
10.	Disintegration tester	QA/DTA/002	Calibrated
11.	Dissolution test apparatus	QC/DIS/001	Calibrated
12.	Sieve Shaker	QC/SSH/001	Qualified
13.	HPLC	QC/HPL/001	Calibrated
14.	UV	QC/UVS/001	Calibrated

8.0 PROCESS FLOWCHART



9.0 BILL OF MATERIALS :

S. No.	Name of the Ingredient	Spec.	Item Code	Quantity/ Tablets (mg)	Std. quantity per 6,00,000 tablets (kg)	OA/ PL (%)	Req. quantity per 6,00,000 tablets (kg)
Dry mixing material:							
1	Ramipril*	BP	RAI/SP/R006	5.100#	3.000	2	3.060#
2	Hydrochlorothiazide^	BP	RAI/SP/H005	12.750#	7.500	2	7.650#
3	Dried Maize Starch**^^	BP	IRM/SP/M001	56.450	33.870	-	33.870
4	Lactose Monohydrate	BP	REX/SP/L003	77.900	46.740	-	46.740
5	Microcrystalline Cellulose PH 102	BP	REX/SP/M010	30.000	18.000	-	18.000
Binder Material:							
6	Gelatin	BP	REX/SP/G001	2.000	1.200	-	1.200
7	Butylated Hydroxy Anisole (BHA)	BP	REX/SP/B002	0.200	0.120	-	0.120
8	Citric Acid Anhydrous	BP	RAI/SP/C016	1.000	0.600	-	0.600
9	Magnesium Oxide Heavy	BP	REX/SP/M021	1.500	0.900	-	0.900
10	Maize Starch	BP	REX/SP/M020	5.000	3.000	-	3.000
11	Erythrosine Supra	IHS	REX/SP/E005	0.100	0.060	-	0.060
12	Purified Water	BP	NA	q.s.	30.000	-	30.000
Theoretical Weight of Dried Granules				**192.000**	**114.990**	-	**115.200**
Lubrication Material:							
13	Sodium Starch Glycollate	BP	REX/SP/S004	5.000	3.000	-	3.000
14	Colloidal Silicon Dioxide	BP	REX/SP/C001	1.000	0.600	-	0.600
15	Stearic Acid	BP	REX/SP/S003	2.000	1.200	-	1.200
Theoretical Weight of the Lubricated granules				**200.000**	**119.790**	-	**120.000**
Theoretical weight of Compressed tablet				**200.000**	**119.790**	-	**120.000**

Generic name	RAMITHIAZIDE 5/12.5
Protocol No.	PVR-R09

10.0 MANUFACTURING PROCESS DETAILS:

10.1. SIFTING:

Step No.	Name of Ingredient	Specified in Approved BMR	Observation		
			Batch No.:		
			GF201004	GF201207	GF210317
1.	Sift Ramipril, Hydrochlorthiazide, Dried Maize starch, Lactose monohydrate, Microcrystalline Cellulose PH102 through 40#.	Mesh size of sieve (40 #)	40#		
		Sieve Integrity Check before use	OK		
		Sieve Integrity Check after use	OK		
2	Sift Sodium Starch Glycollate and Magnesium Stearate through 60#	Mesh size of sieve (60 #)	60#		
		Sieve Integrity Check Before use	OK		
		Sieve Integrity Check after use	OK		
3	Sift Colloidal Silicon Dioxide through 30#	Mesh size of sieve (30 #))	30#		
		Sieve Integrity Check Before use	OK		
		Sieve Integrity Check after use	OK		

10.2 DRY MIXING:

Specified in approved BMR	Setting Time	Observations		
		Batch No.:		
		GF201004	GF201207	GF210317
Transfer the sifted Dried maize starch followed by Ramipril, Hydrochlorothiazide, Microcrystalline Cellulose PH 102 and finally lactose into the RMG/Mass mixer. Mix for 10 minute with impeller at slow speed and chopper 'off '.	10 Min.	Transfered the sifted Dried maize starch followed by Ramipril, Hydrochlorothiazide, Microcrystalline Cellulose PH 102 and finally lactose into the RMG/Mass mixer. Mixed for 10 minute with impeller at slow speed and chopper 'off '.		

10.2 BINDER PREPARATION:

Specified in approved BMR	Setting Time	Observations		
		Batch No.:		
		GF201004	GF201207	GF210317
0.900 Kg of Magnesium Oxide Heavy and mix with 3.000 Kg of Purified Water to form a homogeneous suspension with continuous mixing.	----	0.900 Kg of Magnesium Oxide Heavy and mix with 3.000 Kg of Purified Water to form a homogeneous suspension with continuous mixing.		
Take 18.000 Kg of Purified Water in Paste Kettle and heat till reaches 95^{0}C and dissolve Butylated Hydroxy anisole (BHA), Citric Acid Anhydrous and Erythrosine Supra followed by Gelatin and Maize starch to form a Homogeneous paste with continuous mixing.	95^{0}C	Take 18.000 Kg of Purified Water in Paste Kettle and heat till reaches 95^{0}C and dissolve Butylated Hydroxy anisole (BHA), Citric Acid Anhydrous and Erythrosine Supra followed by Gelatin and Maize starch to form a Homogeneous paste with continuous mixing.		

10.2 WET GRANULATION:

Specified in approved BMR	Setting Time	Observations		
		Batch No.:		
		GF201004	GF201207	GF210317
Add binder solution into RMG/Mass mixer take 1 min for binder addition with impeller slow speed and Chopper OFF.	1 min	Added binder solution into RMG/Mass mixer take 1 min for binder addition with impeller slow speed and Chopper OFF.		
After binder addition allow mixing for 5 minutes. If required allow mixing for 5 min or till required consistency of granules obtained with impeller at slow speed and chopper at slow speed.	1 min	After binder addition allowed to mixing for 5 minutes with impeller at slow speed and chopper at slow speed and got the granules at desirable level.		

10.2 DRYING AND SIFTING:

Specified in approved BMR	Setting Time	Observations		
		Batch No.:		
		GF201004	GF201207	GF210317
Load the wet mass into the FBD bowl/ Tray drier tray and air dry the wet mass till solvent smell vanishes.	----	Load the wet mass into the FBD bowl/ Tray drier tray and air dry the wet mass till solvent smell vanishes.		
Load the wet mass into the cleaned FBD bowl Dry at inlet temperature 50-55°c till the LOD reached up to 2.2% w/w.	1 min	Load the wet mass into the cleaned FBD bowl Dry at inlet temperature 50-55°c. LOD Limit: 1.5-2.2% w/w.		

Sift the dried granules through 20 # sieve. Record the observation.	--	Sifted the dried granules through 20 # sieve.
Mill the oversized granules through 1.5 mm multi mill screen fitted with (knives forward medium speed) followed by sifting through 20# sieve on vibrating sifter and collect the sifted granules in double polythene lined cleaned HDPE containers, record the weights.	---	Milled the oversized granules through 1.5 mm multi mill screen fitted with (knives forward medium speed) followed by sifting through 20# sieve on vibrating sifter and collected the sifted granules in double polythene lined cleaned HDPE containers, record the weights.

10.2 BLENDING & LUBRICATION:

Specified in approved BMR	Setting Time	Observations		
		Batch No.:		
		GF201004	GF201207	GF210317
Blending				
Load the dried and sifted granules, sifted Sodium Starch Glycollate and Colloidal Silicon Dioxide in to the blender and mix at 8 rpm for 15 minutes	20 Min. at 10 RPM	Loaded the dried and sifted granules, sifted Sodium Starch Glycollate and Colloidal Silicon Dioxide in to the blender and mixed at 8 rpm for 15 minutes.		
Lubrication				
Take 5.000 Kg of Pre-Lubricated blend and mix sifted Magnesium Stearate into it then Load into above Pre-lubricated blend and mix for further 2 minutes at 8 RPM	5 min. at 10 RPM	5.000 Kg of Pre-Lubricated blend taken and mixed with sifted Magnesium Stearate and loaded into above Pre-lubricated blend and mixed for further 2 minutes at 8 RPM		

11.0 COMPRESSION: (Machine Setting)

Machine Description		Setting as per Approved BMR	Batch No.:		
			GF201004	GF201207	GF210317
Compression machine type		27 Station Double Rotary	27 Station Double Rotary		
Punch Description	Upper punch	7.93 mm Circular shaped flat faced beveled edge punches.	7.93 mm Circular shaped flat faced beveled edge punches.		
	Lower punch	7.93 mm Circular shaped flat faced plain punches.	7.93 mm Circular shaped flat faced plain punches.		
	Dies	7.93 mm suitable for above punches	7.93 mm suitable for above punches		
Tooling Type		D-Tooling	D-Tooling		

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11.1 PRE-COMPRESSION:

Note: As per the protocol Pre-compressed tablets analyzed 1st batch only.

11.2 COMPRESSION (Speed Challenge Test):

Sr. No.	Parameters	Parameters as per approved BMR	Observation			
			B. No.: GF201004			
			Low speed		High Speed	
			RPM: 10		RPM: 25	
			LHS		RHS	
1	Description	Pink coloured, circular shaped, uncoated tablet with breakline on one side and plain on other side	OK	OK	OK	OK
2	Weight of 27 Tablets	5.400 g ± 3.0 % (5.238 g to 5.562 g)	5.409 gm	5.403 gm	5.398 gm	5.406 gm
3	Average weight (mg)	200.000 mg ± 3.0 % (194.000 mg – 206.000 mg)	200mg	200mg	200mg	200mg
4	Uniformity of weight Tablets	200.000 mg ± 5.0 % (190.000 mg – 210.000 mg)	193, 207	196, 208	194, 207	193, 208
5	Hardness (Kg)	NLT 3.0 Kg (To be established)	6.0kg	6.0kg	4.0kg	4.0kg
6	Thickness (mm)	3.20 mm ± 0.3 mm (2.90 mm – 3.50 mm)	3.12mm	3.14mm	3.13mm	3.23mm
7	Friability	NMT 1% w/w	0.03%	0.04%	0.02%	0.02%
8	Disintegration Time	NMT 15 Minutes	02Min 31Sec	02Min 21Sec	02Min 12Sec	02Min 19Sec

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Sr. No.	Parameters	Parameters as per approved BMR	Observation							
			B. No.: GF201207							
			Low speed				High Speed			
			RPM:10				RPM:25			
			LHS				RHS			
1	Description	Pink coloured, circular shaped, uncoated tablet with breakline on one side and plain on other side	OK		OK		OK		OK	
2	Weight of 27 Tablets	5.400 g ± 3.0 % (5.238 g to 5.562 g)	5.414 gm		5.423 gm		5.403 gm		5.412 gm	
3	Average weight (mg)	200.000 mg ± 3.0 % (194.000 mg – 206.000 mg)	201mg		202mg		201mg		201mg	
4	Uniformity of weight Tablets	200.000 mg ± 5.0 % (190.000 mg – 210.000 mg)	193	208	195	206	193	206	195	207
5	Hardness (Kg)	NLT 3.0 Kg (To be established)	3.8kg		4.5kg		4.3kg		4.0kg	
6	Thickness (mm)	3.20 mm ± 0.3 mm (2.90 mm – 3.50 mm)	3.12mm		3.13mm		3.23mm		3.28mm	
7	Friability	NMT 1% w/w	0.03%		0.04%		0.02%		0.02%	
8	Disintegration Time	NMT 15 Minutes	02Min 39Sec		02Min 22Sec		02Min 12Sec		02Min 14Sec	

Sr. No.	Parameters	Parameters as per approved BMR	Observation							
			B. No.: GF210317							
			Low speed				High Speed			
			RPM: 10				RPM: 25			
			LHS				RHS			
1	Description	Pink coloured, circular shaped, uncoated tablet with breakline on one side and plain on other side	OK		OK		OK		OK	
2	Weight of 27 Tablets	5.400 g ± 3.0 % (5.238 g to 5.562 g)	5.419 gm		5.386 gm		5.403 gm		5.426 gm	
3	Average weight (mg)	200.000 mg ± 3.0 % (194.000 mg – 206.000 mg)	201mg		199mg		200mg		201mg	
4	Uniformity of weight Tablets	200.000 mg ± 5.0 % (190.000 mg – 210.000 mg)	198	204	197	210	189	209	188	210

5	Hardness (KP)	NLT 3.0 Kg (To be established)	3.8kg	3.6kg	4.0kg	4.3kg
6	Thickness (mm)	3.20 mm ± 0.3 mm (2.90 mm – 3.50 mm)	3.19mm	3.18mm	3.24mm	3.26mm
7	Friability	NMT 1% w/w	0.04%	0.02%	0.02%	0.03%
8	Disintegration Time	NMT 15 Minutes	02Min 34Sec	02Min 26Sec	02Min 14Sec	02Min 26Sec

11.3 COMPRESSION (At optimum Speed Low Hardness & High Hardness):

Sr. No.	Parameters	Parameters as per approved BMR	Observation							
			B. No.: GF201004							
			Low Hardness				High Hardness			
			RPM:20				RPM:20			
1	Description	Pink coloured, circular shaped, uncoated tablet with breakline on one side and plain on other side	OK		OK		OK		OK	
2	Weight of 27 Tablets	5.400 g ± 3.0 % (5.238 g to 5.562 g)	5.414 gm		5.423 gm		5.403 gm		5.412 gm	
3	Average weight (mg)	200.000 mg ± 3.0 % (194.000 mg – 206.000 mg)	201mg		202mg		201mg		201mg	
4	Uniformity of weight Tablets	200.000 mg ± 5.0 % (190.000 mg – 210.000 mg)	193	208	195	206	193	206	195	207
5	Hardness (KP)	NLT 3.0 Kg (To be established)	3.5kg		3.2kg		3.3kg		3.1kg	
6	Thickness (mm)	3.20 mm ± 0.3 mm (2.90 mm – 3.50 mm)	3.26mm		3.29mm		3.32mm		3.29mm	
7	Friability	NMT 1% w/w	0.03%		0.04%		0.02%		0.02%	
8	Disintegration Time	NMT 15 Minutes	02Min 39Sec		02Min 22Sec		02Min 12Sec		02Min 14Sec	

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Sr. No.	Parameters	Parameters as per approved BMR	Observation							
			B. No.: GF201207							
			Low Hardness				High Hardness			
			RPM: 20				RPM: 20			
1	Description	Pink coloured, circular shaped, uncoated tablet with breakline on one side and plain on other side	OK		OK		OK		OK	
2	Weight of 27 Tablets	5.400 g ± 3.0 % (5.238 g to 5.562 g)	5.414 gm		5.423 gm		5.403 gm		5.412 gm	
3	Average weight (mg)	200.000 mg ± 3.0 % (194.000 mg – 206.000 mg)	201mg		202mg		201mg		201mg	
4	Uniformity of weight Tablets	200.000 mg ± 5.0 % (190.000 mg – 210.000 mg)	193	208	195	206	193	206	195	207
5	Hardness (KP)	NLT 3.0 Kg (To be established)	3.8kg		4.5kg		4.3kg		4.0kg	
6	Thickness (mm)	3.20 mm ± 0.3 mm (2.90 mm – 3.50 mm)	3.12mm		3.13mm		3.23mm		3.28mm	
7	Friability	NMT 1% w/w	0.03%		0.04%		0.02%		0.02%	
8	Disintegration Time	NMT 15 Minutes	02Min 39Sec		02Min 22Sec		02Min 12Sec		02Min 14Sec	

Sr. No.	Parameters	Parameters as per approved BMR	Observation							
			B. No.: GF210317							
			Low Hardness				High Hardness			
			RPM: 20				RPM: 20			
1	Description	Pink coloured, circular shaped, uncoated tablet with breakline on one side and plain on other side	OK		OK		OK		OK	
2	Weight of 27 Tablets	5.400 g ± 3.0 % (5.238 g to 5.562 g)	5.405 gm		5.413 gm		5.408 gm		5.410 gm	
3	Average weight (mg)	200.000 mg ± 3.0 % (194.000 mg – 206.000 mg)	200mg		201mg		200mg		200mg	
4	Uniformity of weight Tablets	200.000 mg ± 5.0 % (190.000 mg – 210.000 mg)	194	207	193	207	195	206	194	206
5	Hardness (KP)	NLT 3.0 Kg (To be established)	3.6kg		3.5kg		3.3kg		4.0kg	
6	Thickness (mm)	3.20 mm ± 0.3 mm (2.90 mm – 3.50 mm)	3.16mm		3.14mm		3.17mm		3.18mm	
7	Friability	NMT 1% w/w	0.02%		0.03%		0.01%		0.02%	
8	Disintegration Time	NMT 15 Minutes	02Min 29Sec		02Min 23Sec		02Min 24Sec		02Min 34Sec	

10.3.4 COMPRESSION (At Optimum Speed Hopper Challenge Test):

Sr. No.	Parameters	Parameters as per approved BMR	Observation		
			B. No.: GF201004		
			RPM: 24		
			Full Hopper	Middle Hopper	Low Hopper
1	Description	Pink coloured, circular shaped, uncoated tablet with breakline on one side and plain on other side	OK	OK	OK
2	Weight of 27 Tablets	5.400 g ± 3.0 % (5.238 g to 5.562 g)	5.402 gm	5.395 gm	5.384 gm
3	Average weight (mg)	200.000 mg ± 3.0 % (194.000 mg – 206.000 mg)	200mg	200mg	199mg
4	Uniformity of weight Tablets	200.000 mg ± 5.0 % (190.000 mg – 210.000 mg)	194 206	193 205	194 206
5	Hardness (KP)	NLT 3.0 Kg (To be established)	3.8kg	4.5kg	4.3kg
6	Thickness (mm)	3.20 mm ± 0.3 mm (2.90 mm – 3.50 mm)	3.12mm	3.13mm	3.23mm
7	Friability	NMT 1% w/w	0.03%	0.04%	0.02%
8	Disintegration Test	NMT 15 Minutes	02Min 39Sec	02Min 22Sec	02Min 12Sec

Sr. No.	Parameters	Parameters as per approved BMR	Observation		
			B. No.: GF201207		
			RPM: 24		
			Full Hopper	Middle Hopper	Low Hopper
1	Description	Pink coloured, circular shaped, uncoated tablet with breakline on one side and plain on other side	OK	OK	OK
2	Weight of 27 Tablets	5.400 g ± 3.0 % (5.238 g to 5.562 g)	5.413 gm	5.428 gm	5.423 gm
3	Average weight (mg)	200.000 mg ± 3.0 % (194.000 mg – 206.000 mg)	201mg	201mg	201mg
4	Uniformity of weight Tablets	200.000 mg ± 5.0 % (190.000 mg – 210.000 mg)	193 205	194 206	196 205
5	Hardness (KP)	NLT 3.0 Kg (To be established)	3.8kg	3.5kg	3.9kg
6	Thickness (mm)	3.20 mm ± 0.3 mm (2.90 mm – 3.50 mm)	3.16mm	3.18mm	3.24mm

7	**Friability**	NMT 1% w/w	0.03%	0.04%	0.02%
8	**Disintegration Test**	NMT 15 Minutes	02Min 42Sec	02Min 26Sec	02Min 36Sec

Sr. No.	Parameters	Parameters as per approved BMR	Observation					
			B. No.: GF210317					
			RPM: 24					
			Full Hopper		Middle Hopper		Low Hopper	
1	**Description**	Pink coloured, circular shaped, uncoated tablet with breakline on one side and plain on other side.	OK		OK		OK	
2	**Weight of 27 Tablets**	5.400 g ± 3.0 % (5.238 g to 5.562 g)	5.412 gm		5.385 gm		5.387 gm	
3	**Average weight (mg)**	200.000 mg ± 3.0 % (194.000 mg – 206.000 mg)	200mg		199mg		199mg	
4	**Uniformity of weight Tablets**	200.000 mg ± 5.0 % (190.000 mg – 210.000 mg)	194	206	193	205	194	206
5	**Hardness (KP)**	NLT 3.0 Kg (To be established)	3.6kg		3.8kg		3.9kg	
6	**Thickness (mm)**	3.20 mm ± 0.3 mm (2.90 mm – 3.50 mm)	3.19mm		3.23mm		3.27mm	
7	**Friability**	NMT 1% w/w	0.02%		0.04%		0.03%	
8	**Disintegration Test**	NMT 15 Minutes	02Min 29Sec		02Min 33Sec		02Min 26Sec	

12.0 INSPECTION

Parameter	Specified	Observation		
		Batch No.:		
		GF201004	GF201207	GF210317
Equipment Name	Inspection Machine	Inspection Machine		
Equipment ID No.	PD/INB/001	PD/INB/001		
No. of Rejected Tablets	To be recorded	1300 Nos	2200 Nos	900 Nos

13.0 PACKING PROCESS:

13.1 BILL OF PACKING MATERIALS:

Material Name	Item code	UOM	Req. Qty. for 6.0 Lac	Issued Qty.
252 mm Ramithiazide 5/12.5 Printed foil	PPF/SP/R009	Kg	45.000	45.000
252 mm Alu Alu Base foil	PPF/SP/A019	Kg	150.000	150.000
3x10'S Ramithiazide 5/12.5mg Carton	PPC/SP/R010	No	20000	20000
Ramithiazide Printed Leaflet	PPL/SP/R002	No	20000	20000
Shrink Sleeves (PVC)	PPS/SP/P001	No	2000	2000
5 Ply 390x390x430 mm GHPL Printed Shipper	PPS/SP/G002	No	75	75
3' GHPL Printed Bopp Tape	PPB/SP/B002	No	3	3
3' Plain BOPP Tape	PPR/SP/S001	Mtrs	300	300
Strapping role.	NA	No	91	91

13.2 PACKING VALIDATION:

Parameters	Specified	Observation			
		Batch No.:			
		GF201004	GF201207		GF210317
		Low speed/ Low temp.	Low speed/ High temp.	High speed/ High temp.	High speed/ Low temp.
Machine Speed	To be established	10	10	35	35
Forming / Sealing Temperature	To be established	170°C	220°C	220°C	170°C
Pack Quality	Should be proper	It is Proper	It is Proper	It is Proper	It is Proper
Leak Test	Should be absent	Absent	Absent	Absent	Absent
Printing Details	Should be legible and clear	Legible and Clear	Legible and Clear	Legible and Clear	Legible and Clear
Proper Sealing	Should be proper	It is Proper	It is Proper	It is Proper	It is Proper
Horizontal cutting	Should be OK	Ok	Ok	Ok	Ok
Vertical cutting	Should be OK	Ok	Ok	Ok	Ok
Comments/ Remarks	Complies/does not comply with respected to standards of specification	Complies	Complies	Complies	Complies

Generic name	RAMITHIAZIDE 5/12.5
Protocol No.	PVR-R09

14.0 ANALYTICAL RESULTS:

14.1.1 Analytical Result of Lubricated Blend (For 03 Min)

Test	Limit	Observation					
UNIFORMITY OF BLEND	90.0% to 110.0% of the label claim. RSD NMT 5.0%	Sample No.	Batch No.:				
			GF201004		GF201207		GF210317
			Ramipril BP			Hydrochlorothiazide BP	
		1	101.88%	101.21%	102.64%	99.75%	100.95%	97.90%
		2	98.39%	97.22%	101.51%	99.51%	98.01%	99.53%
		3	92.23%	98.47%	97.62%	98.41%	99.72%	98.12%
		4	101.87%	102.34%	98.44%	100.40%	100.91%	97.80%
		5	94.07%	101.22%	93.81%	97.72%	98.24%	97.45%
		6	102.96%	96.74%	99.30%	97.39%	99.90%	99.22%
		7	99.77%	100.89%	97.62%	96.54%	97.62%	96.48%
		8	102.55%	103.72%	98.74%	94.62%	97.49%	99.92%
		9	92.93%	98.38%	100.23%	96.22%	96.82%	101.03%
		10	93.84%	100.41%	102.01%	101.29%	99.96%	101.21%
		Min.	**92.23%**	**96.74%**	**93.81%**	**94.62%**	**96.82%**	**96.48%**
		Max.	**102.96%**	**103.72%**	**102.64%**	**101.29%**	**100.95%**	**101.21%**
		Mean	**98.05%**	**100.06%**	**99.19%**	**98.19%**	**98.96%**	**98.87%**
		% RSD	**4.43**	**2.27**	**2.62**	**2.11**	**1.51**	**1.58**
Comments/ Remark	Complies/does not comply with respected to standards	Complies					

14.1.2 Analytical Result of Lubricated Blend (For 04 Min)

Test	Limit	Observation					
UNIFORMITY OF BLEND	90.0% to 110.0% of the label claim. RSD NMT 5.0%	Sample No.	Batch No.:				
			GF201004		GF201207		GF210317
			Ramipril BP			Hydrochlorothiazide BP	
		1	98.43%	96.95%	101.38%	97.84%	99.36%	98.13%
		2	97.18%	98.67%	101.15%	97.70%	97.45%	97.92%
		3	94.71%	94.22%	98.89%	97.69%	98.54%	98.22%
		4	99.37%	98.60%	101.23%	98.13%	101.81%	98.10%
		5	98.20%	97.90%	97.87%	97.14%	101.65%	97.54%
		6	104.47%	103.10%	100.71%	101.11%	100.54%	100.07%
		7	95.52%	100.96%	98.02%	98.18%	97.75%	99.88%
		8	98.86%	94.09%	98.15%	94.79%	97.20%	100.15%
		9	94.69%	102.97%	100.81%	99.79%	102.09%	99.67%
		10	98.57%	95.20%	97.05%	96.34%	102.46%	96.71%
		Min.	**94.69%**	**94.09%**	**97.05%**	**94.79%**	**97.20%**	**96.71%**
		Max.	**104.47%**	**103.10%**	**101.45**	**101.11%**	**102.46%**	**100.15%**
		Mean	**98.00%**	**98.27%**	**99.53%**	**97.87%**	**99.89%**	**98.64%**
		% RSD	**2.91**	**3.35**	**1.69**	**1.76**	**2.07**	**1.22**
Comments / Remarks	Complies/does not comply with respected to standards of specification	Complies					

14.1.2 Analytical Result of Lubricated Blend (For 05Min)

Test	Limit	Observation					
UNIFORMITY OF BLEND	90.0% to 110.0% of the label claim. RSD NMT 5.0%	Sample No.	Batch No.:				
			GF201004		GF201207	GF210317	
			Ramipril BP			Hydrochlorothiazide BP	
		1	93.86%	102.05%	97.40%	96.80%	100.34%	97.34%
		2	92.69%	93.88%	98.25%	98.62%	101.65%	98.76%
		3	91.79%	94.10%	104.12%	100.22%	97.45%	100.43%
		4	102.43%	95.09%	98.56%	100.67%	98.94%	101.35%
		5	102.18%	105.38%	98.35%	103.09%	100.52%	100.95%
		6	101.53%	101.56%	97.78%	99.58%	101.52%	97.21%
		7	98.73%	97.95%	98.41%	103.76%	100.69%	99.55%
		8	96.24%	99.78%	98.53%	98.37%	99.33%	99.44%
		9	102.02%	102.53%	98.31%	96.98%	98.35%	97.03%
		10	91.56%	92.99%	100.39%	96.65%	98.99%	98.38%
		Min.	**91.56%**	**92.99%**	**97.40%**	**96.65%**	**97.45%**	**97.03%**
		Max.	**102.43%**	**105.38%**	**104.12%**	**103.76%**	**101.69%**	**101.35%**
		Mean	**97.30%**	**98.53%**	**99.01%**	**99.47%**	**99.78%**	**99.04%**
		% RSD	**4.72**	**4.41**	**1.97**	**2.52**	**1.38**	**1.58**
Comments/ Remark	Complies/does not comply with respected to standards of	Complies					

Generic name	**RAMITHIAZIDE 5/12.5**
Protocol No.	**PVR-R09**

Sr. No.	Parameters		Acceptance Criteria	Observation	
				Batch No. GF201004	
1	Description		Pink colour granules.	Pink colour granules.	
2	LOD		Informative	2.11%	
3	Bulk Density (gm/ml)		Informative	0.3942gm/l	
4	Tapped Density (gm/ml)		Informative	0.4711gm/l	
5	Assay (%)	**Ramipril BP**	90.0% to 110.0 %	100.26%	
		Hydrochlorothiazide BP		99.72%	
6	Sieve Analysis	**60#**	Informative	94.26%	5.74%
		80#		84.12%	15.88%
		100#		81.04%	18.96%
		120#		61.44%	38..56%
Comments / Remarks	Complies/does not comply with respected to standards of specification			complies	

Sr. No.	Parameters		Acceptance Criteria	Observation	
				Batch No. GF201207	
1	Description		Pink colour granules.	Pink colour granules.	
2	LOD		Informative	2.06%	
3	Bulk Density (gm/ml)		Informative	0.3716gm/l	
4	Tapped Density (gm/ml)		Informative	0.4926gm/l	
5	Assay (%)	**Ramipril BP**	90.0% to 110.0 %	99.53%	
		Hydrochlorothiazide BP		99.56%	
6	Sieve Analysis	**60#**	Informative	95.92%	4.08%
		80#		85.26%	14.74%
		100#		81.45%	18.55%
		120#		60.23%	39.77%
Comments / Remarks	Complies/does not comply with respected to standards of specification			Complies	

Sr. No.	Parameters	Acceptance Criteria	Observation
			Batch No. GF210317

Generic name	RAMITHIAZIDE 5/12.5
Protocol No.	PVR-R09

1	Description		Pink colour granules.	Pink colour granules.	
2	LOD		Informative	2.09%	
3	Bulk Density (gm/ml)		Informative	0.37369g/l	
4	Tapped Density (gm/ml)		Informative	0.5026g/l	
5	Assay (%)	**Ramipril BP**	90.0% to 110.0 %	98.74%	
		Hydrochlorothiazide BP		99.70%	
6	Sieve Analysis	**60#**	Informative	94.23%	5.77%
		80#		86.26%	13.74%
		100#		80.73%	19.27%
		120#		60.66%	39.34%
Comments / Remarks	Complies/does not comply with respected to standards of specification			Complies	

14.1.3 Analytical Result of Compression at Different Speed:

Test		Limit	Observation	
			Batch No.: GF201004	
			Low Speed	High Speed
			RPM:10	RPM: 30
Assay %	**Ramipril BP**	90.0% to 110.0 %	99.70%	100.14%
	Hydrochlorothiazide BP		99.76%	99.37%
Comments/ Remarks	Complies/does not comply with respected to standards of specification		**Complies**	**Complies**

Test		Limit	Observation	
			Batch No.: GF201207	
			Low Speed	High Speed
			RPM:	RPM:
Assay %	**Ramipril BP**	90.0% to 110.0 %	99.92%	99.64%
	Hydrochlorothiazide BP		99.93%	99.64%
Comments/ Remarks	Complies/does not comply with respected to standards of specification		**Complies**	**Complies**

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Test		Limit	Observation	
			Batch No.: GF210317	
			Low Speed	High Speed
			RPM:	RPM:
Assay	Ramipril BP	90.0% to 110.0 %	99.67%	99.54%
	Hydrochlorothiazide BP		99.62%	99.39%
Comments/ Remarks	Complies/does not comply with respected to standards of specification		Complies	Complies

14.1.4 Analytical Result of Compression at Different Compression Pressure:

Test		Limit	Observation					
			Batch No.: GF201004					
			Low Hardness			High Hardness		
			RPM:24			RPM: 24		
Dissolution	Ramipril BP	NLT 75.0 %	93.46 %	99.63%	96.29%	93.19%	100.26%	97.79%
	Hydrochlorothiazide BP		93.77 %	98.23%	96.47%	93.63%	97.50%	95.94%
Comments / Remarks	Complies/does not comply with respected to standards of specification		Complies			Complies		

Test		Limit	Observation					
			Batch No.: GF201207					
			Low Hardness			High Hardness		
			RPM: 24			RPM: 24		
Dissolution	Ramipril BP	NLT 75.0 %	91.63%	100.93%	95.72%	93.46%	100.02%	97.07%
	Hydrochlorothiazide BP		91.84%	96.96%	94.15%	94.00%	96.99%	95.13%
Comments / Remarks	Complies/does not comply with respected to standards of specification		Complies					

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Test		Limit	Observation					
			Batch No.: GF210317					
			Low Hardness			High Hardness		
			RPM: 24			RPM: 24		
Dissolution	Ramipril BP	NLT 75.0 %	98.34%	103.09%	100.37%	97.21%	101.90%	99.65%
	Hydrochlorothiazide BP		96.03%	99.84%	98.06%	96.93%	100.11%	98.23%
Comments / Remarks	Complies/does not comply with respected to standards of specification		Complies					

14.1.5 Analytical Result of Compression at Optimum Speed(Hopper Challenge):

Test	Limit	Observation					
		Sample No.	Batch No.: GF201004					
			Full Hopper		Middle Hopper		Low Hopper	
UNIFORMITY OF CONTENT	85.0% to 115.0% of the label claim.	1	94.07%	100.44%	103.19%	102.09%	97.76%	100.39%
		2	90.84%	98.74%	99.13%	96.63%	103.50%	98.81%
		3	99.04%	97.55%	91.61%	96.39%	91.81%	102.45%
		4	93.60%	98.38%	95.10%	102.08%	103.43%	96.26%
		5	99.60%	97.56%	102.08%	97.53%	91.79%	102.27%
		6	102..08%	102.03%	93.03%	103.01%	98.94%	100.11%
		7	99.42%	102.23	102.71%	101.69%	100.61%	98.47%
		8	102.71%	100.03%	103.27%	98.07%	99.18%	95.82%
		9	102.27%	97.33%	93.91%	98.95%	95.36%	97.66%
		10	98.25%	96.29%	105.52%	102.09%	97.55%	98.11%
		Min.	**90.84%**	**96.29%**	**91.61%**	**96.39%**	**91.79%**	**95.82%**
		Max.	**102.71%**	**102.23%**	**105.52%**	**103.01%**	**103.50%**	**102.45%**
		Mean	**98.19%**	**99.06%**	**98.96%**	**99.85%**	**97.99%**	**99.04%**
		% RSD	**4.13**	**2.05**	**4.14**	**2.58**	**4.20**	**2.28**
Comments/ Remarks	Complies / does not comply with respected to standards of specification		Complies					

Generic name	RAMITHIAZIDE 5/12.5
Protocol No.	PVR-R09

Test	Limit	Observation					
UNIFORMITY OF CONTENT	85.0% to 115.0% of the label claim.	Sample No.	Batch No.: GF201207				
			Full Hopper		Middle Hopper		Low Hopper
			Composite		Composite		Composite
		1	100.82%	98.24%	96.03%	98.51%	98.78%	102.26%
		2	93.75%	101.88%	95.66%	96.39%	102.67%	100.88%
		3	98.09%	101.75%	93.11%	97.23%	97.95%	98.83%
		4	94.39%	98.12%	98.87%	102.02%	101.31%	98.19%
		5	94.88%	102.08%	98.82%	99.33%	98.55%	102.00%
		6	102.79%	98.42%	93.19%	100.99%	98.94%	98.49%
		7	100.83%	100.79%	103.72%	97.26%	99.01%	98.47%
		8	94.06%	98.03%	98.55%	97.87%	103.90%	97.93%
		9	95.18%	97.33%	93.91%	99.86%	100.86%	97.54%
		10	101.63%	100.79%	99.15%	100.36%	98.72%	98.18%
		Min.	**93.75%**	**97.33%**	**93.11%**	**96.39%**	**97.95%**	**97.54%**
		Max.	**102.79%**	**102.08%**	**103.72%**	**102.02%**	**103.90%**	**102.26%**
		Mean	**97.64%**	**99.74%**	**97.10%**	**99.27%**	**100.07%**	**99.28%**
		% RSD	**3.66**	**1.88**	**3.44**	**1.70**	**2.00**	**1.76**
Comments/ Remarks		Complies / does not comply with respected to standards of specification				Complies		

Test	Limit	Observation					
UNIFORMITY OF CONTENT	85.0% to 115.0% of the label claim.	Sample No.	Batch No.: GF210317				
			Full Hopper		Middle Hopper		Low Hopper
			Composite		Composite		Composite
		1	101.44%	100.19%	99.45%	99.32%	97.89%	100.14%
		2	100.52%	99.95%	99.32%	96.64%	98.96%	99.84%
		3	98.41%	97.53%	100.51%	96.40%	103.18%	96.81%
		4	99.30%	99.78%	96.76%	98.42%	99.71%	97.70%
		5	95.71%	99.33%	98.30%	97.51%	99.87%	100.03%
		6	98.30%	98.36%	97.56%	98.25%	98.30%	101.12%
		7	103.73%	98.21%	99.78%	100.53%	98.41%	99.51%
		8	98.96%	96.40%	99.54%	101.62%	104.96%	95.83%
		9	97.67%	100.0%	101.27%	99.62%	98.51%	99.43%
		10	98.41%	100.05%	101.89%	98.42%	100.39%	101.66%

		Min.	95.71%	96.40%	96.79%	96.40%	97.89%	95.83%
		Max.	103.73%	100.19%	101.89%	101.62%	104.96%	101.66%
		Mean	99.25%	98.98%	99.44%	98.67%	100.02%	99.21%
		% RSD	2.22	1.30	1.59	1.66	2.31	1.87
Comments/ Remarks		Complies / does not comply with respected to standards of specification				Complies		

14.1.6 Analytical Result of Composite Tablets:

Parameters	Specified	Observation Batch No.: GF201004 Composite Sample
Description	Pink coloured, circular shaped, uncoated tablet with breakline on one side and plain on other side side	Pink coloured, circular shaped, uncoated tablet with breakline on one side and plain on other side on other
Weight of 20 tablets	2.800 g± 3.0 % (2.716 gm to 2.884 gm)	2.788gm
Average weight(mg)	140.000 mg ± 3.0 % (133.000 mg – 147.000 mg	139.4mg
Uniformity of weight	140.00 mg ± 5.0 % (133.000 mg – 147.000 mg)	Min: -1.52% and Max: 2.05%
Thickness	3.40 mm ± 0.2 mm (3.20 mm – 3.60 mm)	Min: 3.35mm to Max: 3.45mm
Hardness (N)	NLT 4.0 Kg (To be established)	4.0kg
Friability	NMT 1% w/w	0.26%
Disintegration Time	NMT 15 Minutes	02Min 16Sec
Average Diameter	6.80 mm ± 0.2mm	6.80mm

Parameters	Specified	Observation Batch No.: GF201207 Composite Sample
Description	Pink coloured, circular shaped, uncoated tablet with breakline on one side and plain on other side side	Pink coloured, circular shaped, uncoated tablet with breakline on one side and plain on other side on other
Weight of 20 tablets	2.800 g± 3.0 % (2.716 gm to 2.884 gm)	2.812gm
Average weight(mg)	140.000 mg ± 3.0 % (133.000 mg – 147.000 mg	140.6mg

Uniformity of weight	140.00 mg ± 5.0 % (133.000 mg – 147.000 mg)	Min: -2.03mm; Max: 1.55mm
Thickness	3.40 mm ± 0.2 mm (3.20 mm – 3.60 mm)	Min: 3.36mm and Max: 3.40mm
Hardness (N)	NLT 4.0 Kg (To be established)	4.5Kg
Friability	NMT 1% w/w	0.30%
Disintegration Time	NMT 15 Minutes	02Min and 25Sec
Average Diameter	6.80 mm ± 0.2mm	Min: 6.80mm and Max: 6.82mm

Parameters	Specified	Observation Batch No.: GF210317 Composite Sample
Description	White to off white coloured, circular shaped, biconvex, uncoated tablet with breakline on one side and plain on other side	White to off white coloured, circular shaped, biconvex, uncoated tablet with breakline on one side and plain on other side
Weight of 20 tablets	2.800 g± 3.0 % (2.716 gm to 2.884 gm)	2.822gm
Average weight(mg)	140.000 mg ± 3.0 % (133.000 mg – 147.000 mg	141.1mg
Uniformity of weight	140.00 mg ± 5.0 % (133.000 mg – 147.000 mg)	Min: -1.04: Max: 2.05mm
Thickness	3.40 mm ± 0.2 mm (3.20 mm – 3.60 mm)	Min: 3.29mm: Max: 3.40mm
Hardness (N)	NLT 4.0 Kg (To be established)	4.5Kg
Friability	NMT 1% w/w	0.25%
Disintegration Time	NMT 15 Minutes	2min and 30Sec
Average Diameter	6.80 mm ± 0.2mm	Min: 6.80mm to Max: 6.83mm

15.0 FINISHED PRODUCT REPORT:

Parameter	Specified	Observation Batch No: GF201004 Composite Sample		
Appearance	Pink coloured, flat, round, beveled edged uncoated tablet with break line on one side and plain on other side.	Pink coloured, flat, round, beveled edged uncoated tablet with break line on one side and plain on other side.		
Identification				
Ramipril BP	The retention time of one of the major peak in the chromatogram of sample preparation corresponds to the peak due to Ramipril in standard preparation as obtained in assay.	Complies		
Hydrochlorothiazide BP	The retention time of one of the major peak in the chromatogram of sample preparation corresponds to the peak due to Hydrochlorothiazide in standard preparation as obtained in assay.	Complies		
Average weight	200.0 mg ± 5.0 % (Limit:190.0 mg to 210.0 mg)	202.95mg		
Uniformity of weight	200.0 mg ± 5.0 % (Limit:190.0 mg to 210.0 mg)	-1.50%	+0.90%	
Dimensions:				
Thickness	3.20 mm ± 0.3 mm (2.90 mm – 3.50 mm)	3.10mm	3.15mm.	3.12mm
Hardness	NLT 3.0 kg	3.9Kg/cm^2		
Diameter	7.90 mm ± 0.2mm	8.02 mm	8.05 mm	8.04 mm
Friability	NMT 1.0 %	0.14%		
Disintegration Time	NMT 15mins	02Min 16Sec		
Dissolution Ramipril BP and Hydrochlorothiazide BP	Not less than 75 % of labeled amount	94.43 % 97.40 %	101.68 % 100.64 %	97.94 % 99.49 %
Uniformity of content Ramipril BP 5 mg and Hydrochlorothiazide BP 12.5 mg	85.0 % to 115.0 % of average value. 85.0 % to 115.0 % of average value.	102.23% 100.93%	104.24% 103.83%	103.26% 99.49%
Assay				
Each uncoated tablet contains: Ramipril BP 5 mg and Hydrochlorothiazide BP 12.5 mg	Not less than 90.0 % and Not more than 110.0 %	99.01% 99.05%		

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Related Substance		
Impurity A	NMT 2.00%	Not Detected(ND)
Impurity D	NMT 6.00%	Not Detected(ND)
Impurity E	NMT 2.00%	Not Detected(ND)
Single Maximum unknown Impurity	NMT 0.5%	Below Detection Limit(BDL)
Total Impurities	NMT 6.0%	Below Detection Limit(BDL)
Microbiological Limits		
Total Aerobic Microbial counts	NMT 1000 cfu/g	20cfu/g
Total Yeasts and Mould Counts	NMT 100 cfu/g	<10cfu/g
E.coli	Should Be absent	Absent
Salmonella	Should Be absent	Absent
S.Aureus	Should Be absent	Absent
P. aeruginosa	Should Be absent	Absent

Parameter	Specified	Observation Batch No: GF201207 Composite Sample		
Appearance	Pink coloured, flat, round, beveled edged uncoated tablet with break line on one side and plain on other side.	Pink coloured, flat, round, beveled edged uncoated tablet with break line on one side and plain on other side.		
Identification				
Ramipril BP	The retention time of one of the major peak in the chromatogram of sample preparation corresponds to the peak due to Ramipril in standard preparation as obtained in assay.	Complies		
Hydrochlorothiazide BP	The retention time of one of the major peak in the chromatogram of sample preparation corresponds to the peak due to Hydrochlorothiazide in standard preparation as obtained in assay.	Complies		
Average weight	200.0 mg ± 5.0 % (Limit:190.0 mg to 210.0 mg)	201.40mg		
Uniformity of weight	200.0 mg ± 5.0 % (Limit:190.0 mg to 210.0 mg)	-1.79%	+1.19%	
Dimensions:				
Thickness	3.20 mm ± 0.3 mm (2.90 mm – 3.50 mm)	3.10mm	3.14mm.	3.12mm
Hardness	NLT 3.0 kg	3.2Kg/cm^2		
Diameter	7.90 mm ± 0.2mm	8.02mm	8.06mm	8.04mm
Friability	NMT 1.0 %	0.18%		

Generic name	**RAMITHIAZIDE 5/12.5**
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Disintegration Time	NMT 15mins	02Min 30Sec		
Dissolution Ramipril BP and Hydrochlorothiazide BP	Not less than 75 % of labeled amount	96.12 %	101.97 %	98.85 %
		96.67%	99.52%	98.13%
Uniformity of content Ramipril BP 5 mg and Hydrochlorothiazide BP 12.5 mg	85.0 % to 115.0 % of average value.	101.61%	103.33%	102.30%
	85.0 % to 115.0 % of average value.	98.66%	102.12%	99.69%
Assay				
Each uncoated tablet contains: Ramipril BP 5 mg and Hydrochlorothiazide BP 12.5 mg	Not less than 90.0 % and Not more than 110.0 %	101.54%		
		98.59%		
Related Substance Impurity A Impurity D Impurity E Single Maximum unknown Impurity Total Impurities	 NMT 2.00% NMT 6.00% NMT 2.00% NMT 0.5% NMT 6.0%	 Not Detected(ND) Not Detected(ND) Not Detected(ND) Below Detection Limit(BDL) Below Detection Limit(BDL)		
Microbiological Limits Total Aerobic Microbial counts Total Yeasts and Mould Counts E.coli Salmonella S.Aureus P. aeruginosa	 NMT 1000 cfu/g NMT 100 cfu/g Should Be absent Should Be absent Should Be absent Should Be absent	 20cfu/g <10cfu/g Absent Absent Absent Absent		

Generic name	**RAMITHIAZIDE 5/12.5**
Protocol No.	**PVR-R09**

Parameter	Specified	Observation Batch No: GF210317 Composite Sample		
Appearance	Pink coloured, flat, round, beveled edged uncoated tablet with break line on one side and plain on other side.	Pink coloured, flat, round, beveled edged uncoated tablet with break line on one side and plain on other side.		
Identification				
Ramipril BP	The retention time of one of the major peak in the chromatogram of sample preparation corresponds to the peak due to Ramipril in standard preparation as obtained in assay.	Complies		
Hydrochlorothiazide BP	The retention time of one of the major peak in the chromatogram of sample preparation corresponds to the peak due to Hydrochlorothiazide in standard preparation as obtained in assay.	Complies		
Average weight	200.0 mg ± 5.0 % (Limit:190.0 mg to 210.0 mg)	201.85mg		
Uniformity of weight	200.0 mg ± 5.0 % (Limit:190.0 mg to 210.0 mg)	-1.56%	+1.90%	
Dimensions:				
Thickness	3.20 mm ± 0.3 mm (2.90 mm – 3.50 mm)	3.10mm	3.15mm.	3.12mm
Hardness	NLT 3.0 kg	3.8Kg/cm^2		
Diameter	7.90 mm ± 0.2mm	7.98mm	8.02mm	8.00mm
Friability	NMT 1.0 %	0.15%		
Disintegration Time	NMT 15mins	02Min 25Sec		
Dissolution Ramipril BP and Hydrochlorothiazide BP	Not less than 75 % of labeled amount	101.54%	104.66%	102.85%
		96.67%	99.52%	98.13%
Uniformity of content Ramipril BP 5 mg and Hydrochlorothiazide BP 12.5 mg	85.0 % to 115.0 % of average value.	101.61%	103.33%	102.30%
	85.0 % to 115.0 % of average value.	98.66%	102.12%	99.69%
Assay				
Each uncoated tablet contains:	Not less than 90.0 % and Not more than 110.0 %	101.52%		

Ramipril BP 5 mg and Hydrochlorothiazide BP 12.5 mg		100.83%
Related Substance Impurity A Impurity D Impurity E Single Maximum unknown Impurity Total Impurities	 NMT 2.00% NMT 6.00% NMT 2.00% NMT 0.5% NMT 6.0%	 Not Detected(ND) Not Detected(ND) Not Detected(ND) Below Detection Limit(BDL) Below Detection Limit(BDL)
Microbiological Limits Total Aerobic Microbial counts Total Yeasts and Mould Counts E.coli Salmonella S.Aureus P. aeruginosa	 NMT 1000 cfu/g NMT 100 cfu/g Should Be absent Should Be absent Should Be absent Should Be absent	 20cfu/g <10cfu/g Absent Absent Absent Absent

Generic name	RAMITHIAZIDE 5/12.5
Protocol No.	PVR-R09

16.0 Deviation and Justification/Corrective Action:

Sr. No.	Deviation details	Justification(s) / Corrective Action(s)	Remarks Acceptable / Not acceptable
1.			
2.		Nil	
3.			

17.0 SUMMARY:

The process validation of Ramithiazide 5/12.5 has been carried out and found satisfactory

18.0 CONCLUSION:

The process of Ramithiazide 5/12.5 with batch no. QF201004, QF201007 and QF210918 have been validated and the results obtained from blending, compression and packing found well with in the limit. Hence the process stands validated and recommend to manufacture as same procedure for further batches.

19.0 REPORT APPROVAL:

The process Validation Report of batch "**RAMITHIAZIDE 5/12.5**" having batch size of 6,00,000 Tablets has been reviewed and complies with requirements.

Prepared By:	
Name: R. Crephen	
Sign / Date: 19/09/2024 Quality Assurance	
Checked and Reviewed By:	
Name: A. VALLARASAN	**Name:** BALASUBRAMANIAN. A
Sign/Date: 19/09/2024 Quality Control	**Sign/Date:** 19/09/2024 Production

Comments: We certify that the process Validation report for "**RAMITHIAZIDE 5/12.5**" having batch size of 6, 00,000 Tablets has been accepted.

Report Approved By:
Name: Dr. S. BALAMURUGAN.
Sign / Date: 19/09/2024 HOD Quality Assurance