Salud Pública
Ministerio de Salud
Gobierno de Chile

GZR/pgg
Nº Ref.:MA816587/16

MODIFICA A ASCEND LABORATORIES S.p.A., RESPECTO DEL PRODUCTO FARMACÉUTICO LOSARTÁN POTÁSICO COMPRIMIDOS RECUBIERTOS 50 mg, REGISTRO SANITARIO Nº F-22000/15

RESOLUCIÓN EXENTA RW N° 23235/16
Santiago, 17 de noviembre de 2016

VISTO ESTOS ANTECEDENTES: la presentación de Ascend Laboratories S.P.A., por la que solicita **modificación del periodo de eficacia** para el producto farmacéutico **LOSARTÁN POTÁSICO COMPRIMIDOS RECUBIERTOS 50 mg**, registro sanitario Nº F-22000/15; el Informe Técnico Nº 2906, emitido por la Unidad de Metodologias Analíticas; y

TENIENDO PRESENTE: las disposiciones del artículo 96º del Código Sanitario; del Reglamento del Sistema Nacional de Control de Productos Farmacéuticos, aprobado por el Decreto Supremo Nº 3 de 2010 del Ministerio de Salud; en uso de las facultades que me confieren los artículos 59º letra b) y 61º letra b), del Decreto con Fuerza de Ley Nº 1, de 2005 y las facultades delegadas por la Resolución Exenta Nº 292 de 12 de febrero de 2014 del Instituto de Salud Pública de Chile, dicto la siguiente:

R E S O L U C I Ó N

1.- AUTORÍZASE para el producto farmacéutico **LOSARTÁN POTÁSICO COMPRIMIDOS RECUBIERTOS 50 mg**, registro sanitario Nº F-22000/15, concedido a Ascend Laboratories S.P.A., un Periodo de eficacia de:

36 meses, almacenado a no más de 25ºC en estuche de cartulina impresa ,que contiene blister pack compuesto por lámina de Aluminio termoformado y sellado con film de aluminio impreso, con folleto de información al paciente ,todo debidamente sellado.

2.- El nuevo periodo de eficacia aprobado deberá consignarse claramente en los rótulos del producto, indicando como "Fecha de Vencimiento", el mes y año de expiración de la eficacia del producto, en todas las series o lotes que se fabriquen con posterioridad a la presente resolución.

3.- DÉJASE ESTABLECIDO que la información evaluada en la solicitud para la aprobación de esta modificación al registro sanitario, corresponde a la entregada por el solicitante, el cual se hace responsable de la veracidad de los documentos que adjunta, conforme a lo dispuesto en el Art.210° del Código Penal y que la información proporcionada deberá estar a disposición de la Autoridad Sanitaria, para su verificación, cuando ésta lo requiera.

4.- DÉJASE ESTABLECIDO que el titular del registro tendrá un plazo de 6 meses a contar de la fecha de la presente resolución para actualizar la información en los anexos del registro que así lo requieran, sin necesidad de solicitar expresamente esta modificación al Instituto.

ANÓTESE Y COMUNÍQUESE

JEFA SUBDEPTO. REGISTRO Y AUTORIZACIONES SANITARIAS
AGENCIA NACIONAL DE MEDICAMENTOS
INSTITUTO DE SALUD PÚBLICA DE CHILE

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ALKEM

ALKEM LABORATORIES LIMITED

STABILITY REPORT FORMAT OF LOSARTAN POTASIUM 50 mg TABLETS
(PROTOCOL NO.: SP/GB/003/13-00)

Product : Losartan Potassium Tablets USP	Batch No. 3121534
Strength : 50 mg	Batch size: 750,000 tablets
Pack : 10's Blister	Mfg. : Jul. 2013
Condition : 40°C± 2°C and 75± 5 % RH	Start date: 19/08/13
Purpose of study : To assign shelf life.	

Sr.No.	Test	Specifications	Station				
			Initial	1M	2M	3M	6M
1.	Description	White coloured, circular, film coated tablets plain on both sides.	Complies	Complies	Complies	Complies	Complies
2.	Dissolution (By HPLC) (Test-2)	Not less than 85% (Q) of the labeled amount of Losartan potassium ($C_{22}H_{22}ClKN_6O$) is dissolved in 30 minutes	103	101	98	100	100
			104	99	96	101	98
			103	101	98	101	103
			104	99	96	102	98
			101	101	99	101	100
			104	100	98	101	100
3.	Organic Impurities (By HPLC, w/w)						
	i) I- H- Dimer	Not more than 0.5 %	BQL	BDL	BDL	BDL	BDL
	ii) 2-H- Dimer	Not more than 0.5%	BQL	BDL	BDL	BDL	BDL
	iii) Total impurities	Not more than 1.0%	BQL	BDL	BDL	BDL	BDL
4.	Assay (By HPLC) (% label claim) Losartan Potassium content Claim 50 mg / tablets	Not less than 95.0% and not more than 105.0 % of the labeled amount of Losartan Potassium ($C_{22}H_{22}ClKN_6O$)	99.9	100.4	99.4	99.3	99.4
5.	Microbial Enumeration Tests and Test for specified microorganisms						
	i) Total aerobic microbial count	Not more than 10^3 cfu/g	30 cfu/g	NA	NA	40 cfu/gm	30 cfu/gm
	ii) total combined mold and yeast count	Not more than 10^2 cfu/g	<10 cfu/g			<10 cfu/gm	<10 cfu/gm
	iii) Pathogens	Absent	absent			absent	absent
		Analysis date	14/08/13	05/10/13	09/11/13	04/12/13	19/03/14

Remarks: Nil

Conclusion: Based on above data, it is concludedthat the above product is stable for 6 month at the storage condition 40 ± 2°C / 75 ± 5%RH.

Prepared By	Checked by
Date 25/03/14	Date 02/03/14

ALKEM

ALKEM LABORATORIES LIMITED

STABILITY REPORT FORMAT OF LOSARTAN POTASIUM 50 mg TABLETS
(PROTOCOL NO.: SP/GB/003/13-00)

Product : Losartan Potassium Tablets USP	Batch No. 3121534
Strength : 50 mg	Batch size: 750,000 tablets
Pack : 10's Blister	Mfg. : Jul. 2013
Condition : 30°C± 2°C and 75± 5 % RH	Start date: 19/08/13
Purpose of study : To assign shelf life.	

Sr.No.	Test	Specifications	Station		
			Initial	3M	6M
1.	Description	White coloured, circular, film coated tablets plain on both sides.	Complies	Complies	Complies
2.	Dissolution (By HPLC) (Test-2)	Not less than 85% (Q) of the labeled amount of Losartan potassium ($C_{22}H_{22}ClKN_6O$) is dissolved in 30 minutes.	103	100	100
			104	100	103
			103	101	103
			104	102	98
			101	100	98
			104	101	103
3.	Organic Impurities (By HPLC, w/w)				
	i) 1- H- Dimer	Not more than 0.5 %	BQL	BDL	BDL
	ii) 2-H- Dimer	Not more than 0.5%	BQL	BDL	BDL
	iii) Total impurities	Not more than 1.0%	BQL	BDL	BDL
4.	Assay (By HPLC) (% label claim) Losartan Potassium content Claim 50 mg / tablets	Not less than 95.0% and not more than 105.0 % of the labeled amount of Losartan Potassium. ($C_{22}H_{22}ClKN_6O$)	99.9	100.5	98.4
5.	Microbial Enumeration Tests and Test for specified microorganisms				
	i) Total aerobic microbial count	Not more than 10^3 cfu/g	30 cfu/g	NA	NA
	ii) total combined mold and yeast count	Not more than 10^2 cfu/g	<10 cfu/g		
	iii) Pathogens	Absent	absent		
		Analysis date	14/08/13	04/12/13	04/03/14

Remarks: Nil

Conclusion: Based on above data, it is concluded that the above product is stable for 6 month at the storage condition 30 ± 2°C / 75 ± 5%RH.

Prepared By	Checked by
Date 25/03/14	Date 27/03/14

ALKEM

ALKEM LABORATORIES LIMITED

STABILITY REPORT FORMAT OF LOSARTAN POTASIUM 50 mg TABLETS
(PROTOCOL NO.: SP/GB/003/13-00)

Product : Losartan Potassium Tablets USP	Batch No. 3121534
Strength : 50 mg	Batch size: 750,000 tablets
Pack : 10's Blister	Mfg. : Jul. 2013
Condition : 25°C± 2°C and 60± 5 % RH	Start date: 19/08/13
Purpose of study : To assign shelf life.	

Sr.No.	Test	Specifications	Station		
			Initial	3M	6M
1.	Description	White coloured, circular, film coated tablets plain on both sides.	Complies	Complies	Complies
2.	Dissolution (By HPLC) (Test-2)	Not less than 85% (Q) of the labeled amount of Losartan potassium ($C_{22}H_{22}ClKN_6O$) is dissolved in 30 minutes.	103	101	98
			104	101	98
			103	101	100
			104	101	98
			101	102	103
			104	101	103
3.	Organic Impurities (By HPLC, w/w)				
	i) 1- H- Dimer	Not more than 0.5 %	BQL	BDL	BDL
	ii) 2-H- Dimer	Not more than 0.5%	BQL	BDL	BDL
	iii) Total impurities	Not more than 1.0%	BQL	BDL	BDL
4.	Assay (By HPLC) (% label claim) Losartan Potassium content Claim 50 mg / tablets	Not less than 95.0% and not more than 105.0 % of the labeled amount of Losartan Potassium. ($C_{22}H_{22}ClKN_6O$)	99.9	99.3	99.0
5.	Microbial Enumeration Tests and Test for specified microorganisms				
	i) Total aerobic microbial count	Not more than 10^3 cfu/g	30 cfu/g	NA	NA
	ii) total combined mold and yeast count	Not more than 10^2 cfu/g	<10 cfu/g		
	iii) Pathogens	Absent	absent		
		Analysis date	14/08/13	04/12/13	04/03/14

Remarks: Nil

Conclusion: Based on above data, it is concluded that the above product is stable for 6 month at the storage condition 25 ± 2°C / 60 ± 5%RH.

Prepared By	Checked by
Date 29/03/14	Date 27/03/14

ALKEM

ALKEM LABORATORIES LIMITED

STABILITY REPORT FORMAT OF LOSARTAN POTASIUM 50 mg TABLETS
(PROTOCOL NO.: SP/GB/003/13-00)

Product : Losartan Potassium Tablets USP	Batch No. 3121470
Strength : 50 mg	Batch size: 750,000 tablets
Pack : 10's Blister	Mfg. : Jul. 2013
Condition : 40°C± 2°C and 75± 5 % RH	Start date: 19/08/13
Purpose of study : To assign shelf life.	

Sr.No.	Test	Specifications	Station				
			Initial	1M	2M	3M	6M
1.	Description	White coloured, circular, film coated tablets plain on both sides.	Complies	Complies	Complies	Complies	Complies
2.	Dissolution (By HPLC) (Test-2)	Not less than 85% (Q) of the labeled amount of Losartan potassium ($C_{22}H_{22}ClKN_6O$) is dissolved in 30 minutes.	102	102	98	100	102
			100	102	103	103	100
			101	102	100	101	99
			101	102	98	103	103
			100	102	103	101	98
			102	102	101	101	101
3.	Organic Impurities (By HPLC, w/w)						
	i) 1- H- Dimer	Not more than 0.5 %	BDL	BDL	BDL	BDL	BDL
	ii) 2-H- Dimer	Not more than 0.5%	0.19	BDL	BDL	BDL	BDL
	iii) Total impurities	Not more than 1.0%	0.19	BDL	BDL	BDL	BDL
4.	Assay (By HPLC) (% label claim) Losartan Potassium content Claim 50 mg / tablets	Not less than 95.0% and not more than 105.0 % of the labeled amount of Losartan Potassium. ($C_{22}H_{22}ClKN_6O$)	100.1	100.5	98.9	100.6	99.0
5.	Microbial Enumeration Tests and Test for specified microorganisms						
	i) Total aerobic microbial count	Not more than 10^3 cfu/g	25 cfu/g	NA	NA	30 cfu/gm	25 cfu/gm
	ii) total combined mold and yeast count	Not more than 10^2 cfu/g	<10 cfu/g			<10 cfu/gm	<10 cfu/gm
	iii) Pathogens	Absent	absent			absent	absent
		Analysis date	29/07/13	03/10/13	09/11/13	04/12/13	20/03/14

Remarks: Nil

Conclusion: Based on above data, it is concluded that the above product is stable for 6 month at the storage condition 40 ± 2°C / 75 ± 5%RH.

Prepared By	Checked by
Date 25/03/14	Date 27/03/14

ALKEM

ALKEM LABORATORIES LIMITED

STABILITY REPORT FORMAT OF LOSARTAN POTASIUM 50 mg TABLETS
(PROTOCOL NO.: SP/GB/003/13-00)

Product : Losartan Potassium Tablets USP	Batch No. 3121470
Strength : 50 mg	Batch size: 750,000 tablets
Pack : 10's Blister	Mfg. : Jul. 2013
Condition : 25°C± 2°C and 60± 5 % RH	Start date: 19/08/13
Purpose of study : To assign shelf life.	

Sr.No.	Test	Specifications	Station		
			Initial	3M	6M
1.	Description	White coloured, circular, film coated tablets plain on both sides.	Complies	Complies	Complies
2.	Dissolution (By HPLC) (Test-2)	Not less than 85% (Q) of the labeled amount of Losartan potassium ($C_{22}H_{22}ClKN_6O$) is dissolved in 30 minutes.	102	99	103
			100	102	102
			101	99	100
			101	102	103
			100	100	98
			102	100	98
3.	Organic Impurities (By HPLC, w/w)				
	i) 1- H- Dimer	Not more than 0.5 %	BDL	BDL	BDL
	ii) 2-H- Dimer	Not more than 0.5%	0.19	BDL	BDL
	iii) Total impurities	Not more than 1.0%	0.19	BDL	BDL
4.	Assay (By HPLC) (% label claim) Losartan Potassium content Claim 50 mg / tablets	Not less than 95.0% and not more than 105.0 % of the labeled amount of Losartan Potassium. ($C_{22}H_{22}ClKN_6O$)	100.1	101.2	98.6
5.	Microbial Enumeration Tests and Test for specified microorganisms				
	i) Total aerobic microbial count	Not more than 10^3 cfu/g	25 cfu/g	NA	NA
	ii) total combined mold and yeast count	Not more than 10^2 cfu/g	<10 cfu/g		
	iii) Pathogens	Absent	absent		
		Analysis date	29/07/13	04/12/13	04/03/14

Remarks: Nil

Conclusion: Based on above data, it is concluded that the above product is stable for 6 month at the storage condition 25 ± 2°C / 60 ± 5%RH.

Prepared By	Checked by
Date 29/03/14	Date 22/03/14

ALKEM

ALKEM LABORATORIES LIMITED

STABILITY REPORT FORMAT OF LOSARTAN POTASIUM 50 mg TABLETS
(PROTOCOL NO.: SP/GB/003/13-00)

Product : Losartan Potassium Tablets USP	Batch No. 3121470
Strength : 50 mg	Batch size: 750,000 tablets
Pack : 10's Blister	Mfg. : Jul. 2013
Condition : 30°C± 2°C and 75± 5 % RH	Start date: 19/08/13
Purpose of study : To assign shelf life.	

Sr.No.	Test	Specifications	Station		
			Initial	3M	6M
1.	Description	White coloured, circular, film coated tablets plain on both sides.	Complies	Complies	Complies
2.	Dissolution (By HPLC) (Test-2)	Not less than 85% (Q) of the labeled amount of Losartan potassium ($C_{22}H_{22}ClKN_6O$) is dissolved in 30 minutes.	102	101	102
			100	101	103
			101	102	98
			101	101	103
			100	101	100
			102	101	100
3.	Organic Impurities (By HPLC, w/w)				
	i) 1- H- Dimer	Not more than 0.5 %	BDL	BDL	BDL
	ii) 2-H- Dimer	Not more than 0.5%	0.19	BDL	BDL
	iii) Total impurities	Not more than 1.0%	0.19	BDL	BDL
4.	Assay (By HPLC) (% label claim) Losartan Potassium content Claim 50 mg / tablets	Not less than 95.0% and not more than 105.0 % of the labeled amount of Losartan Potassium. ($C_{22}H_{22}ClKN_6O$)	100.1	100.9	99.9
5.	Microbial Enumeration Tests and Test for specified microorganisms				
	i) Total aerobic microbial count	Not more than 10^3 cfu/g	25 cfu/g	NA	NA
	ii) total combined mold and yeast count	Not more than 10^2 cfu/g	<10 cfu/g		
	iii) Pathogens	Absent	absent		
		Analysis date	29/07/13	04/12/13	04/03/14

Remarks: Nil

Conclusion: Based on above data, it is concluded that the above product is stable for 6 month at the storage condition 30 ± 2°C / 75 ± 5%RH.

Prepared By	Checked by
Date 28/03/14	Date 27/03/14

ALKEM

ALKEM LABORATORIES LIMITED

STABILITY REPORT FORMAT OF LOSARTAN POTASIUM 50 mg TABLETS
(PROTOCOL NO.: SP/GB/003/13-00)

Product : Losartan Potassium Tablets USP	Batch No. 3120638
Strength : 50 mg	Batch size: 750,000 tablets
Pack : 10's Blister	Mfg. : Mar. 2013
Condition : 40°C± 2°C and 75± 5 % RH	Start date: 16/04/13
Purpose of study : To assign shelf life.	

Sr.No.	Test	Specifications	Station				
			Initial	1M	2M	3M	6M
1.	Description	White coloured, circular, film coated tablets plain on both sides.	Complies	Complies	Complies	Complies	Complies
2.	Dissolution (By HPLC) (Test-2)	Not less than 85% (Q) of the labeled amount of Losartan potassium ($C_{22}H_{22}ClKN_6O$) is dissolved in 30 minutes.	101	105	92	101	99
			101	103	93	105	98
			100	105	90	102	102
			103	106	94	110	99
			97	103	93	103	98
			99	106	96	108	101
3.	Organic Impurities (By HPLC, w/w)						
	i) 1- H- Dimer	Not more than 0.5 %	0.02	BDL	BDL	BDL	BDL
	ii) 2-H- Dimer	Not more than 0.5%	0.05	BDL	BDL	BDL	BDL
	iii) Total impurities	Not more than 1.0%	0.30	BDL	BDL	BDL	BDL
4.	Assay (By HPLC) (% label claim) Losartan Potassium content Claim 50 mg / tablets	Not less than 95.0% and not more than 105.0 % of the labeled amount of Losartan Potassium. ($C_{22}H_{22}ClKN_6O$)	98.4	98.3	96.4	97.6	97.7
5.	Microbial Enumeration Tests and Test for specified microorganisms						
	i) Total aerobic microbial count	Not more than 10^3 cfu/g	25 cfu/g	NA	NA	30 cfu/gm	30 cfu/gm
	ii) total combined mold and yeast count	Not more than 10^2 cfu/g	<10 cfu/g			<10 cfu/gm	<10 cfu/gm
	iii) Pathogens	Absent	absent			absent	absent
		Analysis date	28/03/13	31/05/13	28/06/13	05/08/13	22/11/13

Remarks: Nil

Conclusion: Based on above data, it is concluded that the above product is stable for 6 month at the storage condition 40 ± 2°C / 75 ± 5%RH.

Prepared By	Checked by
Date 22/11/13	Date 28/03/14

ALKEM

ALKEM LABORATORIES LIMITED

STABILITY REPORT FORMAT OF LOSARTAN POTASIUM 50 mg TABLETS
(PROTOCOL NO.: SP/GB/003/13-00)

Product : Losartan Potassium Tablets USP	Batch No. 3120638
Strength : 50 mg	Batch size: 750,000 tablets
Pack : 10's Blister	Mfg. : Mar. 2013
Condition : 25°C± 2°C and 60± 5 % RH	Start date: 16/04/13
Purpose of study : To assign shelf life.	

Sr.No.	Test	Specifications	Station			
			Initial	3M	6M	9M
1.	Description	White coloured, circular, film coated tablets plain on both sides.	Complies	Complies	Complies	Complies
2.	Dissolution (By HPLC) (Test-2)	Not less than 85% (Q) of the labeled amount of Losartan potassium ($C_{22}H_{22}ClKN_6O$) is dissolved in 30 minutes.	101	104	99	100
			101	104	101	98
			100	103	99	100
			103	103	101	100
			97	108	99	98
			99	104	101	100
3.	Organic Impurities (By HPLC, w/w)					
	i) 1- H- Dimer	Not more than 0.5 %	0.02	BDL	BDL	BDL
	ii) 2-H- Dimer	Not more than 0.5%	0.05	BDL	BDL	BDL
	iii) Total impurities	Not more than 1.0%	0.30	BDL	BDL	BDL
4.	Assay (By HPLC) (% label claim) Losartan Potassium content Claim 50 mg / tablets	Not less than 95.0% and not more than 105.0 % of the labeled amount of Losartan Potassium. ($C_{22}H_{22}ClKN_6O$)	98.4	97.0	98.0	100.1
5.	Microbial Enumeration Tests and Test for specified microorganisms					
	i) Total aerobic microbial count	Not more than 10^3 cfu/g	25 cfu/g	NA	NA	NA
	ii) total combined mold and yeast count	Not more than 10^2 cfu/g	<10 cfu/g			
	iii) Pathogens	Absent	absent			
		Analysis date	28/03/13	28/07/13	09/11/13	03/02/14

Remarks: Nil

Conclusion: Based on above data, it is concluded that the above product is stable for 9 month at the storage condition 25 ± 2°C / 60 ± 5%RH.

Prepared By	Checked by
Date 25/03/14	Date 27/03/14

ALKEM

ALKEM LABORATORIES LIMITED

STABILITY REPORT FORMAT OF LOSARTAN POTASIUM 50 mg TABLETS
(PROTOCOL NO.: SP/GB/003/13-00)

Product : Losartan Potassium Tablets USP	Batch No. 3120638
Strength : 50 mg	Batch size: 750,000 tablets
Pack : 10's Blister	Mfg. : Mar. 2013
Condition : 30°C± 2°C and 75± 5 % RH	Start date: 16/04/13
Purpose of study : To assign shelf life.	

Sr.No.	Test	Specifications	Station			
			Initial	3M	6M	9M
1.	Description	White coloured, circular, film coated tablets plain on both sides.	Complies	Complies	Complies	Complies
2.	Dissolution (By HPLC) (Test-2)	Not less than 85% (Q) of the labeled amount of Losartan potassium ($C_{22}H_{22}ClKN_6O$) is dissolved in 30 minutes.	101	104	101	100
			101	106	100	98
			100	110	99	99
			103	110	100	100
			97	104	99	98
			99	105	101	99
3.	Organic Impurities (By HPLC, w/w)					
	i) 1- H- Dimer	Not more than 0.5 %	0.02	BDL	BDL	BDL
	ii) 2-H- Dimer	Not more than 0.5%	0.05	BDL	BDL	BDL
	iii) Total impurities	Not more than 1.0%	0.30	BDL	BDL	BDL
4.	Assay (By HPLC) (% label claim) Losartan Potassium content Claim 50 mg / tablets	Not less than 95.0% and not more than 105.0 % of the labeled amount of Losartan Potassium. ($C_{22}H_{22}ClKN_6O$)	98.4	96.7	97.9	100.3
5.	Microbial Enumeration Tests and Test for specified microorganisms					
	i) Total aerobic microbial count	Not more than 10^3 cfu/g	25 cfu/g	NA	NA	NA
	ii) total combined mold and yeast count	Not more than 10^2 cfu/g	<10 cfu/g			
	iii) Pathogens	Absent	absent			
		Analysis date	28/03/13	28/07/13	09/11/13	03/02/14

Remarks: Nil

Conclusion: Based on above data, it is concluded that the above product is stable for 6 month at the storage condition 30 ± 2°C / 75 ± 5%RH.

Prepared By	Checked by
Date 25/03/14	Date 27/03/14