

ESTUDIO DE ESTABILIDAD

HIDROCLOROTIAZIDA COMPRIMIDOS 50 mg

Subdepartamento Registros y Autorizaciones Sanitarias

${\sf HIDROCLOROTIAZIDA\ COMPRIMIDOS\ 50\ mg}$

Estudio de estabilidad

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I. PROTOCOLO

Se realizó una evaluación de la estabilidad de tres lotes de HIDROCLOROTIAZIDA COMPRIMIDOS 50 mg fabricados por HOLDEN MEDICAL LABORATORIES PVT. LTD., utilizando materia prima suministrada por CTX Life Sciences Pvt. LTD. El estudio se llevará a cabo a dos tiempos y condiciones ambientales.

A continuación los lotes a analizar:

Lote	Fecha de	Tamaño de lote	Tiempo de Estudio		
	manufactura	(comprimidos)	Inicio	Final	Final
				(Tiempo real)	(Acelerado)
HM12B10	02-2012	1.000.000	14/02/2012	13/02/2015	14/08/2012
HM12B11	02-2012	1.000.000	14/02/2012	13/02/2015	14/08/2012
HM12B12	02-2012	1.000.000	16/02/2012	15/02/2015	16/08/2012

1. Condiciones

El estudio se realizó almacenando muestras, en las siguientes condiciones de temperatura y humedad relativa:

	Estudio Acelerado	Estudio a tiempo real
Temperatura	40°C ± 2°C	30°C ± 2°C
Humedad	75 % ± 5 % H. R.	65 % ± 5 % H. R

2. Tipo de envase

a) Estuche de cartulina impresa que contiene Blister Aluminio/PVC, más folleto de información al paciente, todo debidamente rotulado y sellado.



Estudio de estabilidad

3. Análisis realizados y frecuencia de testeo:

a) Estudio acelerado

Parámetros medidos	Inicial	3 meses	6 meses
Descripción	٧	٧	٧
Identificación	٧	٧	٧
Desintegración	٧	٧	٧
Disolución	٧	٧	٧
Sustancias Relacionadas	٧	٧	٧
Valoración	٧	٧	٧

b) Estudio a tiempo real

Parámetros medidos	Inicial	3 M	6 M	9 M	12 M	24 M	36 M
Descripción	٧	٧	٧	٧	٧	٧	٧
Identificación	٧	٧	٧	٧	٧	٧	٧
Desintegración	٧	٧	٧	٧	٧	٧	٧
Disolución	٧	٧	٧	٧	٧	٧	٧
Sustancias Relacionadas	٧	٧	٧	٧	٧	٧	٧
Valoración	٧	٧	٧	٧	٧	٧	٧

NOTA: **v** = Parámetro debe ser medido.



Estudio de estabilidad

4. Especificaciones del producto terminado para estabilidad

Test	Especificaciones	Método
Descripción	Comprimido blanco circular, plano sin recubrimiento, con	Inspección
	ranura en uno sólo de sus lados.	visual
Identificación	Espectro muestra y estándar similares.	UV
Tiempo de	No más de 15 minutos	USP <701>
desintegración		
Disolución	No menor a 70% en 45 minutos	UV
Sustancias	Impurezas individuales: No mayor que 1,0%	HPLC
Relacionadas	Total de impurezas: No mayor que 2,5%	
Valoración	Límites: 92,5% a 107,5% de la cantidad declarada	UV



HOLDEN MEDICAL LABORATORIES PVT. LTD. Plot No: C35, C36 & C37, Malegaon MIDC, Sinnar, Nashik -422113. India.

STABILITY STUDY PROTOCOL For Hydrochlorothiazide Tablets BP 50 mg

Protocol No. : SSP/I/95

Issued on: 14/02/12

7. TEST TO BE CARRIED OUT WITH SPECIFICATION:

Sr. No.	Test	Limit
1,	Description	White circular, flat, uncoated, tablets having break line on one side and plain on other side.
2.	Identification By TLC	To comply as per BP
3.	Disintegration Test	NMT 15 min.
4.	Dissolution	NLT 70%.
5,	Related Substances	To comply as per BP
6.	Assay Hydrochlorothiazide BP	-92.5 % to 107.5 %



II. <u>FÓRMULA CUALI-CUANTITA</u>



HOLDEN MEDICAL LABORATORIES PVT. LTD.
Plot No: C35, C36 & C37, Malegaon MIDC, Sinnar, Nashik -422113. India.

STABILITY STUDY PROTOCOL For

Hydrochlorothiazide Tablets BP 50 mg

Protocol No.: SSP/I/95

Issued on: 14/02/12

6. OUALITATIVE AND QUANTITATIVE FORMULA:

Sr. No.	Name of ingredients	Specification	Quantity (mg/Tablet)	Quantity in kg For 10.00 Lac Tablets
1.	Hydrochlorothiazide*	BP	50.000	50.000
2.	Dibasic Calcium Phosphate	BP	36.000	36.000
3.	Maize Starch **	BP	56.000	56.000
4.	Sodium Starch Glycollate	BP	2.000	2.000
5.	PVPK-30	BP	2.100	2.100
6.	Sodium Benzoate	BP	0.120	0.120
7.	Purified Talc	BP	2.500	2.500
8.	Magnesium Stearate	BP	1.280	1.280
9.	Purified Water***	BP,	qs	qs
Fotal V	Veight (in kg)			150.00
Averag	ge Weight of Tablet (in mg)			150.00

- * Quantity of Hydrochlorothiazide BP (API) will be added as per potency.
- ** Quantity of Maize starch BP will be added as per Loss on Drying (LOD).
- *** Purified Water will not be present in final formula.

III. <u>RESULTADOS</u>

a) Estudio de estabilidad acelerado:

Nam	e of Manufacturer :	HOLDEN MEDICAL LABO	ORATORIES PVT. I	LTD.			
City	\$	Nashik (Maharashtra State)					
Cour	itry :	India					
Prod	uct Name	Hydrochlorothiazide Tablets E	3P 50 mg	Stability In	itiation	14/02/1	2
Bate	h No.	HM12B10		Stability To	ermination	14/08/12	2
Batc	h Size	10.00 Lac Tablets		Stability St	orage Conditions	At 40°C	± 2°C & R.H: 75% ± 5%
Mfg.	Date	Feb.2012				Blister Pack	
Exp. Date		Jan.2015		Mode of Packing		10 X 10 Tablets	
Desc	ription	White circular, flat, uncoated,	tablets having break I	ine on one side	e and plain on other side.		
Sr. No.	Parameters	Limits	Initial		3 Months		6 Months
1	Physical Appearance	As per Description	As per Descr	iption	No Change		No Change
2	Identification By TLC	To comply as per BP	Complie	s	Complies		Complies
3	Disintegration time	NMT 15.0 min	2.00 mir	1	4.20 min		5.30 min
4	Dissolution	NLT 70.0%	98.8% to 10	0.1%	96.4% to 99.2%		95.7% to 97.6%
5	Related Substance Individual Impurity: Total Impurities:	To Comply as per BP	Complie Complie		Complies Complies		Complies Complies
6	Assay: Hydrochlorothiazide BP 50 mg/Tab	92.5 % to 107.5 %	99.2%		98.5%		96.8%
Conc	lusion	Hydrochlorothiazide Tablets found stable kept under recom	BP 50 mg, Batch No mended storage condi	tions.	the accelerated stability stu	dy for this b	eatch is completed & it is
Prep:	nared By :	Attested & Approved By:					

Estudio de estabilidad

STABILITY DATA (ACCELERATED STABILITY)

Name of Ma	nufacturer :	HOLDEN MEDICAL LABORATORIES PVT. LTD.
City : Nashik (Maharashtra State)		Nashik (Maharashtra State)
Country	:	India

Prod	uct Name	Hydrochlorothiazide Tablets BP 50 mg		Stability Initiation	14/02/12	
Batch No.		HM12B11		Stability Termination	14/08/12	
Batc	h Size	10.00 Lac Tablets		Stability Storage Conditions	At 40°C ± 2°C & R.H: 75% ± 5%	
Mfg.	Date	Feb.2012		Made of Dealth	Blister Pack	
Exp.	Date	Jan.2015		Mode of Packing	10 X 10 Tablets	
Desc	ription	White circular, flat, uncoated,	tablets having break line on one	side and plain on other side.		
Sr. No.	Parameters	Limits	Initial	3 Months	6 Months	
1	Physical Appearance	As per Description	As per Description	No Change	No Change	
2	Identification By TLC	To comply as per BP	Complies	Complies	Complies	
3	Disintegration time	NMT 15.0 min	3.00 min	4.10 min	6.25 min	
4	Dissolution	NLT 70.0%	95.4% to 97.7%	93.8% to 95.2%	92.1% to 94.5%	
5	Related Substance Individual Impurity: Total Impurities:	To Comply as per BP	Complies Complies	Complies Complies	Complies Complies	
6	Assay: Hydrochlorothiazide BP 50 mg/Tab	92.5 % to 107.5 %	97.8%	95.2%	94.4%	
Conc	clusion	Hydrochlorothiazide Tablets stable kept under recommende		B11, the accelerated stability study for	or this batch is completed & it is fo	

Prepared By:	Attested & Approved By:	
NOV	Approved By:	
	(QA Manager)	

Estudio de estabilidad

STABILITY DATA (ACCELERATED STABILITY)

Name of Manufacturer :	HOLDEN MEDICAL LABORATORIES PVT. LTD.
City :	Nashik (Maharashtra State)
Country :	India

Prod	luct Name	Hydrochlorothiazide Tablets I	3P 50 mg	Stability Initiation	16/02/12			
Bate	h No.	HM12B12		Stability Termination	16/08/12			
Batch Size Mfg. Date Exp. Date		10.00 Lac Tablets		Stability Storage Conditions	At 40°C ± 2°C & R.H: 75% ± 5%			
		Feb.2012			Blister Pack			
		Jan.2015		Mode of Packing	10 X 10 Tablets			
Desc	ription	White circular, flat, uncoated, tablets having break line on one side and plain on other side.						
Sr. No.	Parameters	Limits	Initial	3 Months	6 Months			
1	Physical Appearance	As per Description	As per Description	No Change	No Change			
2	Identification By TLC	To comply as per BP	Complies	Complies	Complies			
3	Disintegration time	NMT 15.0 min	4.00 min	4.20 min	6.15 min			
4	Dissolution	NLT 70.0%	94.9% to 96.3%	93.5% to 94.7%	92.2% to 93.8%			
5	Related Substance Individual Impurity: Total Impurities:	To Comply as per BP	Complies Complies	Complies Complies	Complies Complies			
6	Assay: Hydrochlorothiazide BP 50 mg/Tab	92.5 % to 107.5 %	98.4%	97.9%	97.2%			
Conc	clusion	Hydrochlorothiazide Tablets stable kept under recommende	BP 50 mg, Batch No. HM121 ed storage conditions.	312, the accelerated stability study f	or this batch is completed & it is for			

Prepared By :	Attested & Approved By:	
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	(QA Manager)	

Estudio de estabilidad

b) Estudio de estabilidad a tiempo real:

	STABILITY DATA (REAL TIME STABILITY)
A	L LABORATORIES PVT. LTD.

Name of Manufacturer	HOLDEN MEDICAL LABORATORIES PVT, LTD.
City	Nashik (Maharashtra State)
Country	India

uct Name	Hydrochlorothiaz	ide Tablets BP 50	0 mg		Stabil	lity Initiation		14/02/12	14/02/12		
n No.	HM12B10				Stability Termination			13/02/15			
Batch Size 10.00 Lac Tablets Stability Storage conditions Mfg. Date Feb.2012 Exp. Date Jan.2015 Stability Storage conditions Mode of Packing				Stability Storage conditions			At 30°C	At 30°C ± 2°C & R.H. 65% ± 5%			
					100,000,000,000						
					10 X 10 Tablets						
ription	White circular, fla	at, uncoated, table	ets having break	k line on o	one side	e and plain on	other side.				
Parameters	Limits	Initial	3 Months	6 Months		9 Months	12 Months	18 Months	24 Months	36 Months	
Physical Appearance	As per description	As per Description	No Change	No Change		No Change	No Change	No Change	No Change	No Chang	
Identification By TLC	To comply as per BP	Complies	Complies	Complies		Complies	Complies	Complies	Complies	Complies	
Disintegration time	NMT 15.0 min	2.00 min	2.15 min	2.30 min		3.00 min	3.25 min	3.55 min	4.10 min	6.00 min	
Dissolution	NLT 70.0%	98.8% to 100.1%	98.2% to 99.5%			95.7% to 98.9%	95.3% to 98.6%	94.5% to 97.4%	93.4% to 96.5%	93.0% to 96.2%	
Related Substance Individual Impurity: Total Impurities:	To comply as per BP	Complies Complies	Complies Complies	100000000000000000000000000000000000000	20000	Complies Complies	Complies Complies	Complies Complies	Complies Complies	Complies Complies	
Assay: Hydrochlorothiazide BP 50 mg/Tab	92.5% to 107.5%	99.2%	98.6%			97.9%	97.5%	97.2%	96.7%	96.2%	
H	h No. h Size Date Date Date ription Parameters Physical Appearance Identification By TLC Disintegration time Dissolution Related Substance Individual Impurity: Total Impurities: Assay: Hydrochlorothiazide	h No. HM12B10 h No. HM12B10 h Size 10.00 Lac Tablets Date Feb.2012 Date Jan.2015 ription White circular, flat Parameters Limits Physical As per description Identification To comply as per BP Disintegration time NMT 15.0 min Dissolution NLT 70.0% Related Substance Individual Impurity: Total Impurities: Assay: Hydrochlorothiazide BP 50 me/Tab 10.00 Lac Tablets Tocomplets To comply as per BP	h No. HM12B10 h Size 10.00 Lac Tablets Date Feb.2012 Date Jan.2015 ription White circular, flat, uncoated, table Parameters Limits Initial Physical As per description Description Identification By TLC To comply as per BP Disintegration time NMT 15.0 min 2.00 min Dissolution NLT 70.0% 98.8% to 100.1% Related Substance Individual Impurity: Total Impurities: Assay: P2.5% to 107.5% Hydrochlorothiazide BP 50 mg/Tab	h No. HM12B10 h Size 10.00 Lac Tablets Date Feb.2012 Date Jan.2015 ription White circular, flat, uncoated, tablets having breat Parameters Limits Initial Months Physical As per As per Description Change Identification By TLC Disintegration time NMT 15.0 min 2.00 min 2.15 min Dissolution NLT 70.0% 98.8% to 100.1% 99.5% Related Substance Individual Impurity: Total Impurities: Assay: Hydrochlorothiazide BP 50 mg/Tab	h No. HM12B10 h Size 10.00 Lac Tablets Date Feb.2012 Date Jan.2015 ription White circular, flat, uncoated, tablets having break line on order than the properties of the pr	h No. HM12B10 h Size 10.00 Lac Tablets Date Feb.2012 Mode ription White circular, flat, uncoated, tablets having break line on one side Parameters Limits Initial As per As per No No Change Change Identification By TLC Disintegration time NMT 15.0 min Dissolution NLT 70.0% Related Substance Individual Impurity: Total Impurities: Assay: Hydrochlorothiazide BP 50 me/Tab Mode Stabii Stabii Stabii As par As per No No No Change Complies Complies Complies	h No. HM12B10 h Size 10.00 Lac Tablets Date Feb.2012 Date Tiption White circular, flat, uncoated, tablets having break line on one side and plain on Parameters Limits Initial As per As per No No No No No Appearance description By TLC Disintegration time NMT 15.0 min Dissolution NLT 70.0% Related Substance Individual Impurity: Total Impurities: Assay: Hydrochlorothiazide BP 50 mg/Tab No Occupiles Stability Terminat Stability Storage of Stability Storage of Stability Storage of Mode of Packing Mode of Packing Mode of Packing As per No	h No. HM12B10 Bize 10.00 Lac Tablets Date Feb.2012 Date Jan.2015 Tiption White circular, flat, uncoated, tablets having break line on one side and plain on other side. Parameters Limits Initial As per Appearance As per Description Description To comply as per BP Disintegration time NMT 15.0 min Dissolution NLT 70.0% Related Substance Individual Impurity: Total Impurities: Assay: Hydrochlorothiazide By 50 me/Tab Stability Storage conditions Stability Storage conditions Mode of Packing Mode of Packing Mode of Packing Mode of Packing As ber As per No No No No No Change Change Formula Stability Storage conditions Mode of Packing Mode of Packing As per No No Change Change Formula Stability Storage conditions Mode of Packing Mode of Packing Mode of Packing Formula Stability Storage conditions Mode of Packing As per No No Change Change Formula Stability Storage conditions Mode of Packing Mode of Packing Formula Stability Storage conditions Mode of Packing Mode of Packing Formula Stability Storage conditions Mode of Packing Formula Stability Storage conditions Mode of Packing Mode of Packing Formula Stability Storage conditions Mode of Packing Mode of Packing Formula Stability Storage conditions Mode of Packing Mode of Packing Formula Stability Storage conditions Mode of Packing Formula Stability Storage conditions As per No No Change Complies Complies Complies	h No. HM12B10 h	h No. HM12B10 h No. HM12B10 h Stability Termination Stability Storage conditions At 30°C ± 2°C & R.H. Blister Pack 10 X 10 Tablets To comply as per BP Disintegration time NMT 15.0 min Dissolution NLT 70.0% Related Substance Individual Impurity: Total Impurities: To comply as per BP Complies Complies	

Prepared By:	Attested By & Approved By		
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Estudio de estabilidad

STABILITY DATA (REAL TIME STABILITY)

Name of Manufacturer	HOLDEN MEDICAL LABORATORIES PVT. LTD.	
City	Nashik (Maharashtra State)	
Country	India	

Prod	luct Name	Hydrochlorothiazid	e Tablets BP 50) mg		Stability Initiation	on	14/02/12	14/02/12		
Bate	h No.	HM12B11			i.	Stability Termin	ation	13/02/15			
Bate	h Size	10.00 Lac Tablets Stability				Stability Storage	conditions	At 30°C ±	At 30°C ± 2°C & R.H. 65% ± 5% Blister Pack		
Mfg	Date Feb.2012				Mode of Packing		77531111777716.00				
Exp.	Date	Jan.2015				Mode of Packing	,	10 X 10 T	10 X 10 Tablets		
Desc	ription	White circular, flat,	uncoated, table	ets having break	k line on one	e side and plain on	other side.				
Sr. No	Parameters	Limits	Initial	3 Months	6 Months	9 Months	12 Months	18 Months	24 Months	36 Months	
1	Physical Appearance	As per description	As per Description	No Change	No Change	No Change	No Change	No Change	No change	No change	
2	Identification By TLC	To comply as per BP	Complies	Complies	Complie	s Complies	Complies	Complies	Complies	Complies	
3	Disintegration time	NMT 15.0 min	3.00 min	3.25 min	3.45 mir	4.00 min	4.20 min	4.35 min	4.55 min	5.10 min	
4	Dissolution	NLT 70.0%	95.4% to 97.7%	95.0% to 97.2%	94.7% to 96.3%	93.5% to 95.8%	92.3% to 95.5%	92.0% to 95.2%	91.9% to 94.7%	90.6% to 94.0%	
5	Related Substance Individual Impurity: Total Impurities:	To comply as per BP	Complies Complies	Complies Complies	Complie Complie	0.0 1.0 mm (m.) (m.) (m.) (m.)	Complies Complies	Complies Complies	Complies Complies	Complies Complies	
6	Assay: Hydrochlorothiazide BP 50 mg/Tab		97.8%	97.4%	97.2%	96.5%	96.0%	95.4%	95.0%	94.6%	
Con	clusion	Hydrochlorothiaz packaging is 36 mo conditions.	ide Tablets BP onth. The real ti	50 mg, Batch me stability stu	No. HM12 dy of this ba	B11, The period of atch is completed a	shelf life prop and it is found	osed in storage stable under re	e condition is in commended sto	the original orage	

Prepared By :	Attested By & Approved By	
arm	Approved By	
	(QA Manager)	

Estudio de estabilidad

STABILITY DATA (REAL TIME STABILITY)

Name of Manufacturer	HOLDEN MEDICAL LABORATORIES PVT, LTD.	
City	Nashik (Maharashtra State)	
Country	India	

Prod	luct Name	Hydrochlorothiazid	e Tablets BP 50) mg		Stability Initiat	on	16/02/12	16/02/12		
Bate	h No.	THITTEDIE				Stability Termi	nation	15/02/15	15/02/15 At 30°C ± 2°C & R.H. 65% ± 5%		
Bate	h Size					Stability Storag	e conditions	At 30°C ±			
Mfg. Date		Feb.2012			Mode of Packin	a	Blister Pa				
Exp.	. Date	Jan.2015	.2015				5	10 X 10 Tablets			
Desc	cription	White circular, flat,	uncoated, table	ets having breal	k line on one	side and plain on	other side.				
Sr. No	Parameters	Limits	Initial	3 Months	6 Months	9 Months	12 Months	18 Months	24 Months	36 Months	
1	Physical Appearance	As per description	As per description	No Change	No Change	No Change	No Change	No Change	No change	No change	
2	Identification By TLC	To comply as per BP	Complies	Complies	Complie	s Complies	Complies	Complies	Complies	Complies	
3	Disintegration time	NMT 15.0 min	4.00 min	4.30 min	5.15 min	5.20 min	5.35 min	5.55 min	6.00 min	6.25 min	
4	Dissolution	NLT 70.0%	94.9% to 96.3%	94.5% to 96.0%	94.2% to 95.8%	93.8% to 95,4%	93.4% to 95.1%	93.1% to 94.8%	92,7% to 93.9%	91.3% to 93.6%	
5	Related Substance Individual Impurity: Total Impurities:	To comply as per BP	Complies Complies	Complies Complies	Complies Complies		Complies Complies	Complies Complies	Complies Complies	Complies Complies	
6	Assay: Hydrochlorothiazide BP 50 mg/Tab		98.4%	98.2%	97.9%	97.7%	97.5%	97.1%	96.8%	96.4%	
Con	relusion	Hydrochlorothiaz packaging is 36 mc conditions.	ide Tablets BF onth. The real ti	50 mg, Batch me stability stu	No. HM121 dy of this ba	B12, The period of the is completed a	shelf life propo and it is found s	osed in storage table under rec	condition is in ommended sto	the original rage	

Prepared By :	Attested By & Approved By
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Estudio de estabilidad

IV. DISCUSIÓN

De acuerdo a los resultados obtenidos en el Estudio de Estabilidad, tanto Acelerado como a Tiempo Real de los lotes HM12B10, HM12B11 y HM12B12, se puede verificar que los lotes estudiados no muestran deterioro físico o químico en el envase utilizado (Blister Aluminio/PVC). No se evidencia una disminución significativa en la valoración del activo, y los parámetros analizados se mantuvieron dentro de los límites especificados, durante 36 meses en el estudio a tiempo real y durante 6 meses en el estudio acelerado.

V. CONCLUSIÓN

Basado en los datos adquiridos de los estudios de estabilidad a tiempo real y acelerado, se concluye que el producto analizado es estable por un periodo de 36 meses si se almacena en su envase original cerrado, a una temperatura no mayor a $30^{\circ}\text{C} \pm 2^{\circ}\text{C}$ y una humedad ambiental de $65\% \pm 5\%$.

VI. ESPECIFICACIÓN DE LA VIDA ÚTIL

Se propone un periodo de eficacia para HIDROCLOROTIAZIDA COMPRIMIDOS 50 mg de 36 meses a partir de su fecha de fabricación almacenándolo en su envase original (Estuche de cartulina impresa que contiene Blíster Aluminio/PVC), más folleto de información al paciente, todo debidamente rotulado y sellado, a una temperatura ambiente no mayor a 30°C ± 2°C, protegido de la luz y la humedad.

