

OPKO CHILE S.A.

ESTUDIO DE ESTABILIDAD

DOLERTAB CÁPSULAS 200 MG



DOLERTAB CÁPSULAS 200 MG ESTUDIO DE ESTABILIDAD PROTOCOLO DE ESTABILIDAD

1. INTRODUCCION

Con el fin de estudiar la estabilidad de CELECOXIB CÁPSULAS 200 mg, fue realizado el siguiente estudio, de acuerdo con los requerimientos de la OMS, a través de un estudio de estabilidad acelerado y un estudio de estabilidad a largo plazo de 24 meses.

Esto se requiere para proveer evidencia de como la calidad del producto terminado varía en el tiempo bajo la influencia de factores ambientales tales como temperatura y humedad y también permitir recomendar una condición de almacenamiento y establecer un periodo de eficacia.

2. ALCANCE

Este protocolo brinda detalles sobre la generación de datos de estabilidad en el material de envase primario para DOLERTAB CÁPSULAS 200 mg, tres lotes comerciales fabricados en BAROQUE PHARMACEUTICALS PVT. LTD. Este protocolo se ha preparado con la marca comercial del producto y es aplicable a todas las marcas comerciales y así como el nombre genérico de los productos que tengan la misma fórmula y material de envase.

Nombre y país del Fabricante del Producto Terminado:

SHARON BIO-MEDICINE LIMITED

Add: Selaqui Industrial Area Dehradun Uttarakhand 248001, India.

Nombre y país del Fabricante del Principio Activo:

AARTI DRUGS LTD.

Add: Plot. No. W-60(B) W-61 (B) W-62(B) W-71 (B) W-72 (B) W-73(B), MIDC, TARAPUR, DIST THANE 401506 MAHARASHTRA STATE, INDIA.

Nombre y país de la planta que realiza el Estudio de Estabilidad:

SHARON BIO-MEDICINE LIMITED

Add: Selaqui Industrial Area Dehradun Uttarakhand 248001, India.



CONDICIONES DEL ESTUDIO DE ESTABILIDAD

Tabla 1: Detalle de los lotes:

Lote N°	Fecha de Fabricación	Tamaño de Lote	Tiempo	de Estudio
			Inicio Final	
AEC5001A	Mayo 2015	110.000 Cápsulas	01/jun/2015	01/dic./2017
AEC5002A	Mayo 2015	110.000 Cápsulas	01/jun/2015	01/dic./2017
AEC5003B	Mayo 2015	110.000 Cápsulas	01/jun/2015	01/dic./2017

Tabla 2: Detalle del material de Envase Primario

Lote N°	Tipo de Envase					
AEC5001A	blíster de PVC-PVDC incoloro/Aluminio					
AEC5002A	impreso					
AEC5003B						

Diseño de estabilidad:

El diseño del estudio de estabilidad de DOLERTAB CÁPSULAS 200 mg se ha planeado de la siguiente forma:

Tabla 3:

Condiciones	Temperatura	Humedad Relativa		
Condición 1: Acelerada	40°C <u>+</u> 2°C	75% <u>+</u> 5% HR		
Condición 2: Largo plazo	30°C <u>+</u> 2°C	65% <u>+</u> 5% HR		



Tabla 4:

N°	Condiciones (meses)	0	3	6	9	12	18	24
1	Acelerada	Х	Х	Х	NA	NA	NA	NA
	40°C <u>+</u> 2°C/75% + 5% HR							
2	Largo Plazo	Х	Х	Х	Х	Х	Х	Х
	30°C <u>+</u> 2°C/65% <u>+</u> 5% HR							



 Tabla 5: Se detallan las especificaciones del producto terminado a continuación:

ANÁLISIS	ESPECIFICACIONES	MÉTODO
DESCRIPCIÓN	Cápsula dura N° 2 de gelatina con tapa color rojo oscuro y cuerpo color blanco que contiene polvo color blanco.	Inspección visual
IDENTIFICACIÓN DE CELECOXIB (Por Valoración)	El tiempo de retención del peak principal del cromatograma de la preparación de la valoración debe corresponder al peak de la preparación estándar.	Método In House Técnica de Cuantificación HPLC
PESO PROMEDIO DE LAS CÁPSULAS LLENAS	333,0 mg ± 3,0% (323,01 mg – 342,99 mg)	Gravimétrico
PESO PROMEDIO DEL CONTENIDO DE LA CÁPSULA	270,0 mg ± 3,0% (261,90 mg – 278,10 mg)	Gravimétrico
DISOLUCIÓN (por UV)	No menos de 80% (Q) de la cantidad declarada de Celecoxib se disuelve en 60 minutos. Aparato: N°2 (paleta) Velocidad: 50 rpm Nivel I: (0,04 M fosfato trisódico dodecahidrato pH 12,0 con 1% Lauril Sulfato de Sodio 1%), No menos de 80% (Q) de la cantidad declarada de Celecoxib es disuelta en 60 minutos. Nivel II: Fluido gástrico simulado USP (incluidas pepsina), No menos de 80% (Q) de la cantidad declarada de Celecoxib es disuelta en 60 minutos. (Proceder para análisis Nivel II (S1, S2 & S3) solamente si el criterio para en nivel I no cumple	Método In House Técnica de Cuantificación UV
UNIFORMIDAD DE DOSIS POR VARIACIÓN DE PESO	AV ≤ L1 = 15,0	USP <905>



DEL CONTENIDO DE LA CÁPSULA		
SUSTANCIAS RELACIONADAS	Impureza A: no más de 0,2% Impureza desconocida mayor: no más de 0,2% Impurezas totales: no más de 1,5%	Método In House Técnica de cuantificación HPLC
VALORACIÓN DE CELECOXIB	Teórico: 200 mg CELECOXIB/ cápsula Límites: 190 – 210 mg CELECOXIB/ cápsula 95,0 – 105,0% de la cantidad declarada	Método In House Técnica de cuantificación HPLC
TIPO DE ENVASE	Estuche de cartulina que contiene envase blíster de PVC- PVDC incoloro/Aluminio impreso, más folleto de información al paciente, todo debidamente rotulado	Inspección visual



DOLERTAB CÁPSULAS 200 MG ESTUDIO DE ESTABILIDAD DECLARACION DE FÓRMULA CELECOXIB CÁPSULAS 200 MG

Cada Cápsula contiene:

INGREDIENTES	CANTIDAD (mg)
Celecoxib	200,0
Lactosa Monohidrato	43,15
Croscarmelosa Sódica	3,0
Povidona K-30	6,75
Lauril Sulfato de Sodio	8,10
Estearato de Magnesio	9,0

COMPOSICIÓN DE LA CÁPSULA:

Composición de la tapa de color Rojo

Gelatina

Metilparabeno de Sodio

Propilparabeno de Sodio

Agua Purificada

Carmoisina

Amarillo Crepúsculo

Ponceau 4R

Dioxido de Titanio

Composición del cuerpo de color Blanco

Gelatina

Metilparabeno de Sodio

Propilparabeno de Sodio

Agua Purificada

Dioxido de Titanio

Materia prima utilizada y posteriormente eliminada durante el proceso de fabricación:

Agua Purificada



REPORTE DEL ESTUDIO DE ESTABILIDAD EN CONDICIONES ACELERADAS



: 200 mg

: q.s.

ESTUDIO DE ESTABILIDAD

ACCELERATED STABILITY SUMMARY REPORT

Sharon Product Name

: Celecoxib Capsule 200 mg

Batch Size Label claim

: 1.10 Lac.Capsules (0.151 Lac pack) Each Hard gelatin Capsule contains

Celecoxib

Excipients

Packing details

: Blister Pack (3x10's)

Protocol Reference : SS19017, Rev-00

Batch No. Overages

: AEC5001A : Nil

Manufacturing Date

: 05/2015

Expiry Date : 05/2017 Shelf Life : 24 Months

: 01/06/2015

Stability Started on Stability condition

: 40+ 2°C/ 75+ 5% RH

Sr.				Accelerat	ed stability stu	dy results		Remark
No.	Test	Specifications	Initial	Month				
				1 MONTHS	2 MONTHS	3 MONTHS	6 MONTHS	To be
	Refere	nce A.R. NO.	FP150568	SS151097	SS151164	SS151337	SS151952	Recorded
1.	Description	Size "2" Hard Gelatine Capsule dark red cap and white body containing white coloured powder.	Complies	Complies	Complies	Complies	Complies	Complies
2.	Water content (By KF)	Not more than 5 % w/w	1.5 % w/w	1.6 % w/w	1.5 % w/w	1.94 % w/w	1.62 % w/w	Complies
3.	Dissolution (By UV)	Not less than 80 % (Q) of labeled amount of Celecoxib is dissolved in 60 minutes.	89 – 99 %	88 – 92 %	92 – 98 %	93 – 99 %	95 – 98 %	Complies
4.	Assay (By HPLC)	Not less than 90.0 % and not more than 110.0 % of labeled amount of celecoxib.	98.9 %	100.3 %	99.6 %	99.8 %	100 .0 %	Complies
	Related substances (By HPLC) A) Impurity A	A) Not more than 0.2 %	0.09 %	0.08 %	0.08 %	0.08 %	0.08 %	
5.	B) Highest unknown	B) Not more than 0.2 %	0.02 %	0.01%	0.02 %	0.02 %	0.02 %	Complies
	impurity C) Total impurity	C) Not more than 1.5 %	0.13 %	0.12 %	0.13 %	0.13 %	0.1 %	

Equipment I.D.: OQST 06 - 01

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ESTUDIO DE ESTABILIDAD

ACCELERATED STADILITI SUMMART REPURT

Product Name Batch Size

Label claim

Sharon

: Celecoxib Capsule 200 mg

: 1.10 Lac.Capsules (0.151 Lac pack) Each Hard gelatin Capsule contains

Celecoxib

: 200 mg Excipients : q.s.

Packing details : Blister Pack (3x10's)

Protocol Reference : SS19017, Rev-00

Batch No.

: AEC5001A Overages : Nil

Manufacturing Date Expiry Date

: 05/2015 : 05/2017

Shelf Life

: 24 Months : 01/06/2015

Stability Started on

Stability condition

: 40± 2°C/ 75± 5% RH

Sr.	Test Specifications		Accelerated stability study results					
No.		Specifications	Initial	Month				
140.			Initial	1 MONTHS	2 MONTHS	3 MONTHS	6 MONTHS	To be
	Reference A.R. N	O.	FP150568	SS151097	SS151164	SS151337	SS151952	Recorded
6.	** Total Viable aerobic count- Bacteria	Not more than 10 ³ cfu/g	Less than 10cfu/g	NA	NA	NA	Less than 10cfu/g	Complies
7.	**Total Viable aerobic Count- Yeast & mould	Not more than 10 ² cfu/g	Less than 10cfu/g	NA	NA	NA	Less than 10cfu/g	Complies
8.	** Salmonella Escherichia Coli P.Aeruginosa Staphylococcus aureus	Should be absent/10g Should be absent/ g Should be absent/ g Should be absent/ g	Absent	NA	NA	NA	Absent	Complies
Samp	ole withdrawn on :-	NA	09/07/15	30/07/15	03/09/15	03/12/15	NA	
Anal	ysis completed on :		NA	09/08/15	17/08/15	16/09/15	12/12/15	NA

Equipment I.D.: OOST 06 - 01

Remarks : Accelerated stability study of 06 month complies/Does not comply as per specifications

ND: Not detected, NA: Not applicable, (**):Microbial tests are designated as to be optional in the Shelf life specification, NMT: Not more than, NLT: Not Less Than

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ESTUDIO DE ESTABILIDAD

ACCELERATED STABILITY SUMMART REPORT

Product Name

Sharon

: Celecoxib Capsule 200 mg

Batch Size Labet claim : 1.10 Lac.Capsules (0.151 Lac pack) Each Hard gelatin Capsule contains

Celecoxib

Excipients : q.s.

Packing details

: Blister Pack (3x10's Protocol Reference : SS19017, Rev-00

: 200 mg

Equipment I.D.: OQST 06 - 01

Batch No. Overages

: AEC5002A

: Nil

Manufacturing Date : 05/2015 **Expiry Date** : 05/2017 : 24 Months

Shelf Life : 01/06/2015 Stability Started on

Stability condition : 40± 2°C/ 75± 5% RH

Sr.				Accelerat	ed stability stu	dy results	esults	
No.	Test	Specifications	Initial	Month				1
				1 MONTHS	2 MONTHS	3 MONTHS	6 MONTHS	To be
	Referen	ce A.R. NO.	FP150574	SS151096	SS151165	SS151336	SS151951	Recorded
1.	Description	Size "2" Hard Gelatine Capsule dark red cap and white body containing white coloured powder.	Complies	Complies	Complies	Complies	Complies	Complies
2.	Water content (By KF)	Not more than 5 % w/w	1.0 % w/w	1.9 % w/w	1.6 % w/w	1.9 % w/w	1.25 % w/w	Complies
3.	Dissolution (By UV)	Not less than 80 % (Q) of labeled amount of celecoxib is dissolved in 60 minutes.	96 – 101 %	87 – 92 %	93 – 98 %	90 – 97 %	93 – 95 %	Complies
4.	Assay (By HPLC)	Not less than 90.0 % and not more than 110.0 % of labeled amount of celecoxib.	101.9 %	100.1 %	99.2 %	99.4 %	99.4 %	Complies
5.	Related substances (By HPLC) A) Impurity A B) Highest unknown impurity C) Total impurity	A) Not more than 0.2 % B) Not more than 0.2 % C) Not more than 1.5 %	0.09 % 0.08 % 0.21 %	0.09 % 0.01 % 0.13 %	0.08 % 0.02 % 0.12 %	BDL 0.09 % 0.12 %	0.08 % 0.02 % 0.12 %	Complies

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ESTUDIO DE ESTABILIDAD

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ACCELERATED STADILITE SUMMART REPORT

Product Name

: Celecoxib Capsule 200 mg

Batch Size Label claim : 1.10 Lac.Capsules (0.151 Lac pack) Each Hard gelatin Capsule contains

Celecoxib

: 200 mg

Excipients

Packing details Protocol Reference : SS19017, Rev-00

: Blister Pack (3x10's

: q.s.

Equipment I.D.: OOST 06 - 01

Batch No.

: AEC5002A

: Nil

Overages Manufacturing Date

: 05/2015 : 05/2017

Expiry Date Shelf Life

Stability condition

: 24 Months

Stability Started on

: 01/06/2015 : 40± 2°C/ 75± 5% RH

Sr.			Accelerated stability study results						
No.	Test	Specifications	Initial	Month				Remarks	
			Tincian .	1 MONTHS	2 MONTHS	3 MONTHS	6 MONTHS	To be	
	Reference A.R	. NO.	FP150574	SS151096	SS151165	SS151336	SS151951	Recorded	
6.	** Total Viable aerobic count- Bacteria	Not more than 10 ³ efw'g	Less than 10cfu/g	NA	NA	NA	Less than 10cfu/g	Complies	
7.	**Total Viable aerobic Count-Yeast & mould	Not more than 10 ² cfu/g	Less than 10cfu/g	NA	NA	NA	Less than 10cfu/g	Complies	
** Salmonella Should be absent/10g Escherichia Coli Should be absent/ g P.Aeruginosa Should be absent/ g Staphylococcus aureus Should be absent/ g		Absent	NA	NA	NA	Absent	Complies		
Samp	ole withdrawn on :		NA	09/07/15	30/07/15	03/09/15	03/12/15	NA	
Analysis completed on :		NA	09/08/15	17/08/15	16/09/15	12/12/15	NA		

: Accelerated stability study of 06 month complies/Does not comply as per specifications. Remarks

ND: Not detected, NA: Not applicable, (*'):Microbial tests are designated as to be optional in the Shelf life specification, NMT: Not more than, NLT: Not Less Than

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ESTUDIO DE ESTABILIDAD ACCELERATED STABILITY SUMMARY REPORT



Product Name

: Celecoxib Capsule 200 mg

Batch Size Label claim : 1.10 Lac.Capsules (0.151 Lac pack) Each Hard gelatin Capsule contains

Celecoxib

: 200 mg

Excipients

: q.s.

Packing details

: Blister Pack (3x10's

Batch No.

: AEC5003B

Overages Manufacturing Date : Nil : 05/2015

Expiry Date

: 05/2017

Shelf Life

: 24 Months

Stability Started on

: 01/06/2015

Protocol Reference : SS19017,Rev-00 Equipment I.D.: OQST 06 - 01 Stability condition : 40± 2°C/75±5% RH

Sr.	Total	Constellation of the constant		Accelera	ated stability stu	dy results		Remark
No.	Test	Specifications	Initial					
				1 MONTHS	2 MONTHS	3 MONTHS	6 MONTHS	To be
	Ref	erence A.R. NO.	FP150582	SS151023	SS151206	SS151330	SS151950	recorded
1.	Description	Size "2" Hard Gelatine Capsule dark red cap and white body containing white coloured powder.	Complies	Complies	Complies	Complies	Complies	Complies
2.	Water content (By KF)	Not more than 5 % w/w	1.6 % w/w	1.8 % w/w	1.4 % w/w	1.8 % w/w	1.75% w/w	Complies
3.	Dissolution (By UV)	Not less than 80 % (Q) of labeled amount of Celecoxib is dissolved in 60 minutes.	97 – 100 %	88 – 93 %	92 – 99 %	91 – 99 %	93 – 95 %	Complies
4.	Assay (By HPLC)	Not less than 90.0 % and not more than 110.0 % of labeled amount of celecoxib.	97.7 %	100.1 %	99.5 %	99.7 %	99.5 %	Complies
5.	Related substances (By HPLC) A) Impurity A B) Highest unknown impurity C) Total impurity	A) Not more than 0.2 % B) Not more than 0.2 % C) Not more than 1.5 %	0.09 % 0.13 % 0.27 %	0.08 % 0.02 % 0.13 %	0.08 % 0.02 % 0.13 %	BDL 0.09 % 0.12 %	0.08% 0.02% 0.1 %	Complies

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: 200 mg

ESTUDIO DE ESTABILIDAD ACCELERATED STABILITY SUMMARY REPORT



Product Name

Packing details

: Celecoxib Capsule 200 mg

Batch Size Label claim : 1.10 Lac.Capsules (0.151 Lac pack) Each Hard gelatin Capsule contains

Celecoxib

Excipients

: q.s. : Blister Pack (3x10's

Protocol Reference : SS19017.Rev-00

Batch No.

: AEC5003B

Overages

: Nil Manufacturing Date : 05/2015

Expiry Date

: 05/2017

Shelf Life

: 24 Months

Stability Started on

: 01/06/2015

Equipment I.D.: OQST 06 - 01 Stability condition : 40± 2°C/ 75± 5% RH

e				Accelerat	ed stability study r	esults		Remarks
Sr. No.	Test	Specifications	Initial	Month				
140.			Initial	1 MONTHS	2 MONTHS	3 MONTHS	6 MONTHS	To be
	Reference A.	R. NO.	FP150582	SS151023	SS151206	SS151330	SS151950	Recorded
6.	** Total Viable aerobic count- Bacteria	Not more than 103cfu/g	Less than 10cfu/g	NA	NA	NA	Less than 10cfu/g	Complies
7.	**Total Viable aerobic Count-Yeast & mould	Not more than 10 ² efu/g	Less than 10cfu/g	NA	NA	NA.	Less than 10cfu/g	Complies
8.	** Salmonella Escherichia Coli P.Aeruginosa Staphylococcus aureus	Should be absent/10g Should be absent/ g Should be absent/ g Should be absent/ g	Absent	NA	NA	NA	Absent	Complies
Samp	ole withdrawn on :		NA	02/07/15	06/08/15	03/09/15	03/12/15	NA
Analy	ysis completed on :		NA	27/07/15	17/08/15	16/09/15	12/12/15 .	NA

Remarks : Accelerated stability study of 06 month complies/Does-not-comply-as per specifications.

ND: Not detected, NA: Not applicable, (*): Microbial tests are designated as to be optional in the Shelf life specification, NMT: Not more than, NLT: Not Less Than

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REPORTE DEL ESTUDIO DE ESTABILIDAD EN CONDICIONES A LARGO PLAZO



ESTUDIO DE ESTABILIDAD LONG TERM STABILITY SUMMARY REPORT

Equipment I.D.: OOST 06 - 03

Sharon **Product Name** Batch Size

Label claim

: Celecoxib Capsule 200 mg

: 1.10 Lac. Capsules (0.151 Lac pack) Each Hard gelatin Capsule contains

Celecoxib

: 200 mg Excipients : q.s.

Packing details : Blister Pack (3x10's) Protocol Reference : SS19017.Rev -00

Batch No.

: AEC5001A Overages : Nil

Manufacturing Date : 05/2015

Expiry Date : 05/2017 Shelf Life : 24 Months

Stability Started on Stability condition

: 30+ 2°C/65+ 5% RH

: 01/06/2015

Sr.				Long ter	rm stability stud	y results		Remark	
No.	Test	Specifications		Month					
			Initial	3 MONTHS	6 MONTHS	9 MONTHS	12 MONTHS	To be	
	Reference A.R. NO.			SS151335	SS151955	SS160268	SS160858	recorded	
1.	Description	Size "2" Hard Gelatine Capsule dark red cap and white body containing white coloured powder.	Complies	Complies	Complies	Complies	Complies	Complies	
2.	Water content (By KF)	Not more than 5 % w/w	1.5 % w/w	1.92 % w/w	1.62 % w/w	2.6 % w/w	2.2 % w/w	Complies	
3.	Dissolution (By UV)	y UV) Not less than 80 % (Q) of labeled amount of Celecoxib is dissolved in 60 minutes.		90 97 %	93 - 96 %	96 - 100 %	95 – 99 %	Complies	
4.	Assay (By HPLC)	Not less than 90.0 % and not more than 110.0 % of labeled amount of celecoxib.	98.9 %	100.0 %	101.0 %	98.9 %	99.53 %	Complies	
5.	Related substances (By HPLC) A. Impurity A B. Highest unknown impurity C. Total impurity	Related substances By HPLC) A. Impurity A B. Highest unknown impurity A) Not more than 0.2 % B) Not more than 0.2 %			0.08 % 0.02 % 0.10 %	0.03 % 0.05 % 0.09 %	ND 0.02 % 0.06 %	Complies	

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ESTUDIO DE ESTABILIDAD LUNG TERM STABILITY SUMMARY REPORT

Equipment I.D.: OOST 06 - 03

Sharon Product Name

Batch Size

: Celecoxib Capsule 200 mg

: 1.10 Lac. Capsules (0.151 Lac pack)

Each Hard gelatin Capsule contains Label claim

Celecoxib : 200 mg

Excipients

: q.s.

Packing details

: Blister Pack (3x10's)

Protocol Reference : SS19017, Rev -00

Batch No.

Overages

: Nil

Manufacturing Date

: 05/2015

Expiry Date Shelf Life

: 05/2017 : 24 Months

: AEC5001A

Stability Started on

: 01/06/2015

Stability condition

: 30± 2°C/ 65± 5% RH

Sr.				Long to	erm stability study	results		Remarks	
No.	Test	Specifications	Initial	Month					
			Illitiai	3 MONTHS	6 MONTHS	9 MONTHS	12 MONTHS	To be	
	Reference A.I	R. NO.	FP150568	SS151335	SS151955	SS160268	SS160858	recorded	
6.	** Total Viable aerobic count- Bacteria	Not more than 103cfu/g	Less than 10cfu/g	NA	NA	NA	Less than 10cfu/g	Complies	
7.	**Total Viable aerobic Count-Yeast & mould	Not more than 10 ² cfu/g	Less than 10cfu/g	NA	NA	NA	Less than 10cfu/g	Complies	
8.	** Salmonella Escherichia Coli P.Aeruginosa S. aureus	Should be absent/10g Should be absent/ g Should be absent/ g Should be absent/ g	Absent	NA	NA	NA	Absent	Complies	
Samp	ole withdrawn on :		· NA	03/09/15	03/12/15	25/02/16	02/06/16	NA	
Anal	Analysis completed on :		NA	16/09/15	12/12/15	10/03/16	21/06/16	NA	

Remarks

: Long term stability study of 30 month complies/Does not comply as per specifications.

ND: Not detected, NA: Not applicable, (**): Microbial tests are designated as to be optional in the Shelf life specification, NMT: Not more than, NLT: Not Less Than

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ESTUDIO DE ESTABILIDAD LONG TERM STABILITY SUMMARY REPORT

Equipment I.D.: OOST 06 - 03

Sharon Product Name

Batch Size

Label claim

: Celecoxib Capsule 200 mg

: 1.10 Lac. Capsules (0.151 Lac pack) Each Hard gelatin Capsule contains

Celecoxib

: 200 mg Excipients : q.s.

Packing details

: Blister Pack (3x10's)

Protocol Reference : SS19017,Rev -00

Batch No.

: AEC5001A

Overages Manufacturing Date

: 05/2015

: Nil

Expiry Date Shelf Life

: 05/2017 : 24 Months

Stability Started on

: 01/06/2015

Stability condition : 30+ 2*C/ 65+ 5% RH

				Long	term stability stu	de monte	
Sr.	Test	Specifications		Long			 Remark
No.	Test	Specifications	Initial		Month		
				18 MONTHS	24 MONTHS	30 MONTHS	To be
	Refer	rence A.R. NO.	FP150568	SS161743	SS170838	SS171623	recorded
1.	Description	Size "2" Hard Gelatine Capsule dark red cap and white body containing white coloured powder.	Complies	Complies	Complies	Complies	Complies
2.	Water content (By KF)	Not more than 5 % w/w	1.5 % w/w	1.5 % w/w	2.13 % w/w	2.12 % w/w	
3.	Dissolution (By UV)	Not less than 80 % (Q) of labeled amount of Celecoxib is dissolved in 60 minutes.	89 – 99 %	96 – 103 %	93 – 101 %	94%,95%,98%, 97%,95%,95% Avg 96 %,	Complies
4.	Assay (By HPLC)	Not less than 90.0 % and not more than 110.0 % of labeled amount of celecoxib.	98.9 %	99.27 %	99.16 %	99.53 %	Complies
5.	Related substances (By HPLC) A) Impurity A B) Highest unknown impurity C). Total impurity	A) Not more than 0.2 % B) Not more than 0.2 % C) Not more than 1.5 %	0.09 % 0.02 % 0.13 %	ND 0.07 % 0.07 %	ND 0.02 % 0.03 %	ND 0.055 % 0.096 %	Complies

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ESTUDIO DE ESTABILIDAD

LUNG TERM STABILITY SUMMARY REPURT

Product Name

: Celecoxib Capsule 200 mg

Batch No.

: AEC5001A

Batch Size

Sharon

: 1.10 Lac. Capsules (0.151 Lac pack)

Overages Manufacturing Date : Nil : 05/2015

Label claim

Each Hard gelatin Capsule contains

Expiry Date

: 05/2017

ł

Celecoxib Excipients

: 200 mg : q.s.

Shelf Life

: 24 Months

Packing details

: Blister Pack (3x10's)

Stability Started on

: 01/06/2015

Protocol Reference : SS19017.Rev -00

Equipment I.D.: OQST 06 - 03

Stability condition

: 30± 2°C/ 65± 5% RH

		Test Specifications Long term stability study results Month		Long term stability study results				
Sr. No.	Test			Remarks				
110.		,	Initial	18 MONTHS	24 MONTHS	30 MONTHS		
	Reference A.F	t. NO.	FP150568	SS161743	SS170838	SS171623	To be recorded	
6. ** Total Viable aerobic count- Bacteria		Not more than 103cfu/g	Less than 10cfu/g	NA	Less than 10cfu/g	Less than 10cfu/g	Complies	
7.	**Total Viable aerobic Count-Yeast & mould	Not more than 10 ² cfu/g	Less than 10cfu/g	NA	Less than 10cfu/g	Less than 10cfu/g	Complies	
8. Escherichia Coli Should be absent/ g P.Aeruginosa Should be absent/ g			Absent	NA	Absent	Absent	Complies	
Sample withdrawn on :		NA	01/12/16	01/06/17	30/11/17	NA .		
Analy	sis completed on :	NA	09/12/16	19/06/17	09/12/17	NA		

ND: Not detected, NA: Not applicable, (**): Microbial tests are designated as to be optional in the Shelf life specification, NMT: Not more than, NLT: Not Less Than

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C. Not more than 1.5 %

ESTUDIO DE ESTABILIDAD

Sharon

LONG TERM STABILITY SUMMARY REPORT

Product Name

: Celecoxib Capsule 200 mg

Batch No.

: AEC5002A

Batch Size Label claim : 1.10 Lac. Capsules (0.151 Lac pack) Each Hard gelatin Capsule contains Overages

: Nil

Celecoxib

: 200 mg

Manufacturing Date Expiry Date : 05/2015 : 05/2017

Excipients

: q.s.

Shelf Life

: 05/2017 : 24 Months

0.12 %

Packing details

: Blister Pack (3x10's

.

Stability Started on

: 01/06/2015

Prot	ocol Reference : SS19017	,Rev-00 Equipmen	nt I.D.: OQST	06-03	Stability co	ondition	: 30± 2°C/ 65±	5% RH
Sr.	Test	Specifications		Long te	rm stability stu	dy results		Remark
No.	Test	Specifications	Initial		M	lonth		
		L		3 MONTHS	6 MONTHS	9 MONTHS	12 MONTHS	To be
	Referen	ice A.R. NO.	FP150574	SS151334	SS151951	SS160267	SS160859	Recorded
1.	Description	Size "2" Hard Gelatine Capsule dark red cap and white body containing white coloured powder.	Complies	Complies	Complies	Complies	Complies	Complies
2.	Water content (By KF)	Not more than 5 % w/w	1.0 % w/w	1.77 % w/w	1.25% w/w	2.4 % w/w	2.7% w/w	Complies
3.	Dissolution (By UV)	Not less than 80 % (Q) of labeled amount of Celecoxib is dissolved in 60 minutes.	96 – 101 %	93 – 102 %	93 – 95 %	97 – 100 %	95 – 98 %	Complies
4.	Assay (By HPLC)	Not less than 90.0 % and not more than 110.0 % of labeled amount of celecoxib.	101.9 %	99.9 %	99.4%	100.1 %	99.16 %	Complies
5.	Related substances (By HPLC) A. Impurity A B. Highest unknown impurity	A. Not more than 0.2 % B. Not more than 0.2 %	0.09 %	BDL 0.09 %	0.08 %	ND 0.04 %	ND 0.04 %	Complies

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0.21%

0.11%

0.1 %

0.04 %

Format No. 134.001.18

C. Total impurity



ESTUDIO DE ESTABILIDAD

Equipment I.D.: OQST 06-03

Sharon

LUNG TERM STABILITY SUMMART REPORT

Product Name

: Celecoxib Capsule 200 mg

Batch Size Label claim : 1.10 Lac. Capsules (0.151 Lac pack)
Each Hard gelatin Capsule contains

Celecoxib

: 200 mg

Excipients

: q.s.

Packing details

: Blister Pack (3x10's

Protocol Reference : SS19017 .Rev-00

Batch No.

: AEC5002A

Overages

: Nil

Manufacturing Date Expiry Date : 05/2015

Shelf Life

: 24 Months

Stability Started on

: 01/06/2015

Stability condition

: 30± 2°C/ 65± 5% RH

e				Long ter	rm stability study resu	ılts		Remarks	
Sr. No	Test S	Specifications	Initial						
140			Initiai	3 MONTHS	6 MONTHS	9 MONTHS	12 MONTHS	To be	
	Reference A.R. NO.		FP150574	SS151334	SS151951	SS160267	SS190859	Recorded	
6.	** Total Viable aerobic count- Bacteria	Not more than 103cfu/g	Less than 10cfu/g	NA	Less than10cfu/g	NA	Less than 10cfu/g	Complies	
7.	**Total Viable aerobic Count-Yeast & mould	Not more than 10 ² cfu/g	Less than 10cfu/g	NA	Less than 10cfu/g	NA	Less than 10cfu/g	Complies	
8.	** Salmonella Escherichia Coli P.Aeruginosa S.aureus	Should be absent /10g Should be absent / g Should be absent / g Should be absent / g	Absent	NA	Absent	NA	Absent	Complies .	
Samp	Sample withdrawn on :		NA	03/09/15	03/12/15	25/02/16	02/06/16	NA	
Analy	sis completed on :		N/A	16/09/15	12/12/15	10/03/16	21/06/16	NA	

Remarks : Lor

: Long Term stability study of 30 month compiles Does not comply as per specifications.

ND: Not detected, NA: Not applicable, (**): Microbial tests are designated as to be optional in the Shelf life specification, NMT: Not more than, NLT: Not Less Than

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ESTUDIO DE ESTABILIDAD

Sharon

Product Name

: Celecoxib Capsule 200 mg

Batch Size Label claim : 1.10 Lac. Capsules (0.151 Lac pack) Each Hard gelatin Capsule contains

Celecoxib

: 200 mg

Excipients

: q.s.

Packing details Protocol Reference : SS19017 ,Rev-00

: Blister Pack (3x10's

Equipment I.D.: OQST 06-03

Batch No.

: AEC5002A

Overages : Nil

Manufacturing Date : 05/2015 : 05/2017

Expiry Date Shelf Life : 24 Months

Stability Started on

Stability condition

: 01/06/2015 : 30± 2°C/ 65± 5% RH

-							
				Long to	erm stability study	y results	Remark
Sr. No.	Test	Specifications			Mor	ıth	Kemark
140.	-		Initial	18 MONTHS	24 MONTHS	30 MONTHS	To be
	Refer	ence A.R. NO.	FP150574	SS161742	SS170839	SS171622	Recorded
1.	Description	Size "2" Hard Gelatine Capsule dark red cap and white body containing white coloured powder.	Complies	Complies	Complies	Complies	Complies
2.	Water content (By KF)	Not more than 5 % w/w	1.0 % w/w	1.6 % w/w	2.10 % w/w	2.47 % w/w	Complies
3.	Dissolution (By UV)	Not less than 80 % (Q) of labeled amount of Celecoxib is dissolved in 60 minutes.	96 – 101 %	97 – 103 %	92 – 102 %	94 – 97 %	Complies
4.	Assay (By HPLC)	Not less than 90.0 % and not more than 110.0 % of labeled amount of celecoxib.	101.9 %	100.23 %	99.0 %	101.62 %	Complies
5.	Related substances (By HPLC) A. Impurity A B. Highest unknown impurity C. Total impurity	A. Not more than 0.2 % B. Not more than 0.2 % C. Not more than 1.5 %	0.09 % 0.08 % 0.21 %	ND 0.07 % 0.07 %	ND 0.02 % 0.03 %	ND 0.055 % 0.095 %	Complies

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ESTUDIO DE ESTABILIDAD

Sharon

LONG TERM STABILITE SUMMART REPORT

Product Name

: Celecoxib Capsule 200 mg

Batch Size Label claim : 1.10 Lac. Capsules (0.151 Lac pack) Each Hard gelatin Capsule contains

Celecoxib

: 200 mg Excipients : q.s.

Packing details

: Blister Pack (3x10's

Protocol Reference : SS19017 ,Rev-00

Batch No.

: AEC5002A

Overages

: Nil

Manufacturing Date

: 05/2015

Expiry Date

: 05/2017 : 24 Months

Shelf Life Stability Started on

: 01/06/2015

Stability condition

: 30± 2°C/ 65± 5% RH

Sr.				Long	term stability study	results		Domonko	
No.	Test	Specifications	Initial	,	Remarks				
140.			Initial	18 MONTHS	24 MONTHS	30 MONTHS		To be	
	Reference A.	R. NO.	FP150574	SS161742	SS170839	SS171622		Recorded	
** Total Vinhle people		Not more than 10 ³ cfu/g	Less than 10cfu/g	NA	Less than 10cfu/g	Less than 10cfu/g		Complies	
7.	7. **Total Viable aerobic Count-Yeast & mould Not more than 16 ² cf		Less than 10cfu/g	NA .	Less than 10cfu/g	Less than 10cfu/g		Complies	
8. Escherichia Coli Should be absent /10g P.Aeruginosa Should be absent / g		Absent	NA	Absent	Absent		Complies		
Samp	le withdrawn on :		NA	01/12/16	01/06/17	30/11/17		NA	
Analy	sis completed on :		NA	09/12/16	20/06/17	09/12/17		NA	

Equipment I.D.: OQST 06-03

: Long Term stability study of 30 month complies/Does not comply as per specifications. Remarks

ND: Not detected, NA: Not applicable, ("):Microbial tests are designated as to be optional in the Shelf life specification, NMT: Not more than, NLT: Not Less Than

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ESTUDIO DE ESTABILIDAD

Sharon

LUNG TERM STADILITT SUMMART REPORT

Product Name

: Celecoxib Capsule 200 mg

Batch Size Label claim : 1.10 Lac.Capsules (0.151 Lac pack) Each Hard gelatin Capsule contains

Celecoxib

Excipients

: Blister Pack (3x10's

Packing details Protocol Reference : SS19017, Rev-00

Equipment I.D.: OQST 06 - 03

: 200 mg

: q.s.

Batch No.

Overages

: AEC5003B : Nil

Manufacturing Date Expiry Date

: 05/2015 : 05/2017

Shelf Life

: 24 Months

Stability Started on : 01/06/2015 Stability condition

: 30± 2°C/ 65± 5% RH

Sr.					Remark			
No.	Test	Test Specifications	Initial		Month			
				3 MONTHS	6 MONTHS	9 MONTHS	12 MONTHS	To be
-	Refe	rence A.R. NO.	FP150582	SS151326	SS151953	SS160302	SS160865	recorded
1.	Description	Size "2" Hard Gelatine Capsule dark red cap and white body containing white coloured powder.	Complies	Complies	Complies	Complies	Complies	Complies
2.	Water content (By KF)	Not more than 5 % w/w	1.6 % w/w	1.73% w/w	1.55% w/w	2.4 % w/w	2.4 % w/w	Complies
3.	Dissolution (By UV)	Not less than 80 % (Q) of labeled amount of Celecoxib is dissolved in 60 minutes.	97 – 100 %	89- 101 %	94– 95 %	96 – 100 %	96 – 100 %	Complies
4.	Assay (By HPLC)	Not less than 90.0 % and not more than 110.0 % of labeled amount of celecoxib.	97.7 %	99.0 %	100.1 %	98.5 %	99.14 %	Complies
5.	Related substances (By HPLC) A. Impurity A B. Highest unknown impurity	A. Not more than 0.2 % B. Not more than 0.2 %	0.09 % 0.13 %	0.09% 0.011 %	0.08 %	0.03 %	ND 0.04%	Complies
	C. Total impurity	C. Not more than 1.5 %	0.27 %	0.11%	0.1 %	0.08 %	0.06%	

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ESTUDIO DE ESTABILIDAD

Equipment I.D.: OQST 06 - 03

Sharon

LUNG TERM STABILITY SUMMARY REPORT

Product Name

: Celecoxib Capsule 200 mg

Batch Size Label claim : 1.10 Lac.Capsules (0.151 Lac pack) Each Hard gelatin Capsule contains

Celecoxib

: 200 mg

Excipients

: q.s.

Packing details

: Blister Pack (3x10's

Protocol Reference : SS19017, Rev-00

Batch No.

Oaten No.

: AEC5003B

Overages Manufacturing Date : Nil : 05/2015

Expiry Date

: 05/2017

Shelf Life

: 24 Months

Stability Started on Stability condition : 01/06/2015 : 30± 2°C/ 65± 5% RH

Sr.		Long term stability study results					Remarks	
No.	Test	Specifications	Initial	Month				Kemarks
140.			Initial	3 MONTHS	6 MONTHS	9 MONTHS	12 MONTHS	To be Recorded
	Reference A.R.	FP150582	SS151326	SS151953	SS160302	SS160865		
6.	** Total Viable aerobic count- Bacteria	Not more than 103cfu/g	Less than 10cfu/g	NA	NA	NA	Less than 10cfu/g	Complies
7.	**Total Viable aerobic Count-Yeast & mould	Not more than 10 ² cfu/g	Less than 10cfu/g	NA	NA	NA	Less than 10cfu/g	Complies
8.	** Salmonella Escherichia Coli P.Aeruginosa Staphylococcus aureus	Should be absent/10g Should be absent/ g Should be absent/ g Snould be absent/ g	Absent	NA	NA	NA	Absent	Complies
Samp	le withdrawn on :		NA	03/09/15	03/12/15	03/03/16	02/06/16	NA
Analy	sis completed on :		NA	16/09/15	12/12/15	10/03/16	21/06/16	NA

Remarks

: Long Term stability study of 30 month complies/Does not comply as per specifications.

ND: Not detected, NA: Not applicable, (**):Microbial tests are designated as to be optional in the Shelf life specification, NMT :Not more than, NLT: Not Less Than

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Sign & Date	Sign & Date	Sign & Date



ESTUDIO DE ESTABILIDAD

Equipment I.D.: OQST 06 - 03

Sharon

LONG TERM STABILITE SUMMART REPORT

Product Name

: Celecoxib Capsule 200 mg

Batch Size Label claim : 1.10 Lac.Capsules (0.151 Lac pack)
Each Hard gelatin Capsule contains

Celecoxib

: 200 mg

Excipients

: q.s.

Packing details

: Blister Pack (3x10's

Protocol Reference : SS19017,Rev-00

Batch No.

Overages

: Nil

Manufacturing Date Expiry Date : 05/2015 : 05/2017

Shelf Life

: 24 Months

: AEC5003B

Stability Started on Stability condition : 01/06/2015 : 30± 2°C/ 65± 5% RH

6				Long term stability study results			Remark
Sr. No.	Test	Specifications	Initial	Month			
				18 MONTHS	24 MONTHS	30 MONTHS	To be
	Reference A.R. NO.		FP150582	SS161738	SS170837	SS171669	recorded
1.	Description	Size "2" Hard Gelatine Capsule dark red cap and white body containing white coloured powder.	Complies	Complies	Complies	Complies	Complies
2.	Water content (By KF)	Not more than 5 % w/w	1.6 % w/w	1.5 % w/w	2.16 % w/w	1.73 % w/w	Complies
3.	Dissolution (By UV)	Not less than 80 % (Q) of labeled amount of Celecoxib is dissolved in 60 minutes.	97 – 100 %	95 – 102 %	92 – 103 %	97 - 103 %	Complies
4.	Assay (By HPLC)	Not less than 90.0 % and not more than 110.0 % of labeled amount of celecoxib.	97.7 %	102.18 %	99.28 %	100.3 %	Complies
5.	Related substances (By HPLC) A. Impurity A B. Highest unknown impurity C. Total impurity	A. Not more than 0.2 % B. Not more than 0.2 % C. Not more than 1.5 %	0.09 % 0.13 % 0.27 %	ND 0.06 % 0.06 %	ND 0.02 % 0.03 %	ND 0.055 % 0.096 %	Complies

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ESTUDIO DE ESTABILIDAD

LUNG TERM STABILITY SUMMARY REPURT

Equipment I.D.: OQST 06 - 03

Product Name

: Celecoxib Capsule 200 mg

Batch Size Label claim

Sharon

: 1.10 Lac.Capsules (0.151 Lac pack) Each Hard gelatin Capsule contains

Celecoxib

: 200 mg

Excipients

: q.s.

Packing details

: Blister Pack (3x10's

Protocol Reference : SS19017, Rev-00

Batch No.

Overages

: Nil

Manufacturing Date

: 05/2015

Expiry Date Shelf Life

: 05/2017 : 24 Months

: AEC5003B

Stability Started on

: 01/06/2015

Stability condition

: 30± 2°C/ 65± 5% RH

e.,	r. Test Specifications		Long term stability study results				
		Specifications	Initial	Month			Remarks
No.			Initial	18 MONTHS	24 MONTHS	30 MONTHS	To be
	Reference A.R.	NO.	FP150582	SS161738	SS170837	SS171669	Recorded
6.	** Total Viable aerobic count- Bacteria	Not more than 103cfu/g	Less than 10cfu/g	NA	Less than 10cfu/g	Less than 10cfu/g	Complies
7.	**Total Viable aerobic Count-Yeast & mould	Not more than 10 ² cfu/g	Less than 10cfu/g	NA	Less than 10cfw/g	Less than 10cfu/g	Complies
8.	** Salmonella Escherichia Coli P.Aeruginosa Staphylococcus aureus	Should be absent/10g Should be absent/ g Should be absent/ g Should be absent/ g	Absent	NA	Absent	Absent	Complies
Samp	le withdrawn on :		. NA	01/12/16	01/06/17	07/12/17	NA
Analysis completed on :		NA	09/12/16	20/06/17	11/12/17	NA	

: Long Term stability study of 30 month complies: Does not comply as per specifications. Remarks

ND: Not detected, NA: Not applicable, (**):Microbial tests are designated as to be optional in the Shelf life specification, NMT: Not more than, NLT: Not Less Than

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EVALUACION Y ANALISIS DE LOS RESULTADOS

De acuerdo a los resultados obtenidos en el estudio de estabilidad Acelerado en condiciones de temperatura y humedad de 40° C \pm 2° C Y 75% \pm 5% H; y estudio de estabilidad a Tiempo real, en condiciones de 30° C \pm 2° C y 65% \pm 5% HR, para los Lotes AEC5001A, AEC5002A, AEC5003B; se puede verificar que los lotes estudiados no muestran deterioro físico o químico en el envase estudiado. No se evidencia una disminución significativa en la valoración del activo y los parámetros analizados se mantuvieron dentro de los límites especificados.

CONCLUSIONES

Basado en los datos adquiridos de los estudios de estabilidad a tiempo real y acelerado, se concluye que el producto DOLERTAB CÁPSULAS 200 mg es estable bajo un estudio de estabilidad de 30 meses, almacenado en su envase original y a una temperatura no mayor a 30º C, protegido del calor, la humedad y la luz.

Se propone periodo de eficacia para DOLERTAB CÁPSULAS 200 MG de 24 meses con una condición de almacenamiento no mayor a 30°C, a partir de su fecha de fabricación.