

DRUG DEVELOPMENT

H and  20    01  **B**ooks

Drug Development & Manufacture for Pharmaceutical Technology Professions

HANDBOOK OF GENERIC DRUG DEVELOPMENT

READY-TO-GO™ SERIES

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DRUG DEVELOPMENT

Hand 20 Books

Drug Development & Manufacture for Pharmaceutical Technology Professions

TECHNICAL FILE



CMC

Part II

STABILITY

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01/99 Part No. HBGDPI-II-V1

DRUG DEVELOPMENT

Hand 20  **Books**

Drug Development & Manufacture for Pharmaceutical Technology Professions

TECHNICAL FILE

GENERIC ACTIFED
Pseudoephedrine 60mg
Triprolidine 2.5 mg
IMMEDIATE RELEASE SCORED TABLETS

Lot: 41B612 ; 10699/19 ; 10699/23 ; 167001/497 ; 167002/497
Lot: BNC644 (200)

STABILITY

May Contain: Stability Indicating Assay Method + Impurity Profile; SI Method Validation; Dissolution Stability Protocol and 25 & 40° C Profile (NLT 3 Pivotal Batches)

e-HANDBOOK of GENERIC DEVELOPMENT Ready-To-Go™ KNOW-HOW SERIES

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Ready-To-Go™

120 plus

KNOW-HOW

Series

Ready-To-Go™

Expedited CMC for e-mail transmission only

A complete set of TESTING Specifications is herewith provided for each strength of the solid oral dosage form.

Pseudoephedrine

60mg

Triprolidine

2.5 mg

IMMEDIATE RELEASE SCORED TABLETS

Part 1 - Manufacturing CMC

- Part II - STABILITY CMC

IAG172-00

e-HANDBOOK of GENERIC DEVELOPMENT KNOW-HOW SERIES

Electronic version

Available on CD ROM DISKETTE and via E-MAIL ATTACHMENT

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The enclosed database is reviewed in **January/April** each year according to the product's update requirements (Stability, Assay, Manufacturing Process update data).

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DRUG DEVELOPMENT

Hand 20  01  **Books**

Drug Development & Manufacture for Pharmaceutical Technology Professions

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PRODUCT MASTER FORMULA

Generic Name: Pseudoephedrine 60mg / Triprolidine 2.5mg Tablets	<h2 style="margin: 0;">IAGIM</h2> Edition No: 02	Signatures ↻ Development	
DEPARTMENT: Granulation & Tableting	Edition Status: Spsds. 01	Validation ↻	
PRECAUTION: Wear mask and gloves CAUTION: 1. Wear Masks with air filters 2. Potent Active Materials	Effective Date: Jan/15/2001 Cat. No: IAG-167-2000	Production ↻ Q.A. ↻	
		R.A. ↻	

CHANGE : No change

Page 1 of 1

BATCH NO.

Weighing Date : _____

Per Unit Dose	Ex-cess	Raw Materials 300 000 units	Per 91.220 Kg					Signatures Weighing Depart.	
			kg	g	mg	L	mL	A	B
PART I									
62.0		Lactose Monohydrate NF (200 mesh)	18	600					
2.5		Triprolidine HCl	0	750					
60.0	6.0	Pseudoephedrine HCl	19	800					
PART II									
60.0		Starch NF	18	000					
PART III									
90.0		Lactose Monohydrate NF (200 mesh)	27	000					
PART IV									
-		Purified Water USP (85-95°C)	23	000					
2.3		PVP K-30 (Povidone USP)	0	690					
14.0	1.4	Starch NF	4	620					
PART V									
-		Purified Water USP q.s. (up to 6.0 kg)	qs	000					
PART VI									
5.6		Ac-Di-Sol™ (Croscarmellose Sodium NF)	1	680					
3.6		Magnesium Stearate NF	1	080					
300.0	7.4	Theoretical End Volume	<u>91</u>	<u>220</u>					

10% Excess Starch NF added to compensate the loss of water during the granulation/drying process

ED. NO: 02 Replaces 01	Effective Date: Jan / 15 / 2001	APPROVED:			
Ed. Status : 02 - EU		Department	R&D	RA	QC / QA

STABILITY STUDIES -GENERIC ACTIFED TABLETS 60/2.5 mg**PSEUDOEPHEDRINE ASSAY**

Batch number: AIG/167-02-597
Batch size: 180,000 tablets
Manufacturing date: 28.04.1997.
Storage conditions: 25°C (±2°) / 60%RH (±5%)
Packaging: Blister: PVC / PVdC film laminate into Aluminium foil.
HPLC I Assay: Pseudoephedrine 60mg/Tab - Percentage of labelled Amount

Page 1 of 4

Parameter 🔄	Test	Specification	T₀		6 month		12 months		24 months		36 months	
Analysis date 🔄	Method	Criteria Accept -Reject	21. May 1997		23. Nov 1997		24. May 1998		20. May 1999		27. May 2000	
Appearance Description Score	PSD-01400-0	White, round film-coated tablets 9.2 mm diameter, scored on one the face and plain on the reverse side.	Color conforms No spots or marks on smooth surface		Color conforms No spots or marks on smooth surface		Color conforms No spots or marks on smooth surface		Color conforms No spots or marks on smooth surface		Color conforms No spots or marks on smooth surface	
(%) Dissolution labeled amount	PSD-01402	NLT 75% of the labelled amount dissolves within 45 minutes	102.9		102.4		99.7		98.1		101.1	
Assay I (%)	PSD-01404	95.0 - 105.0% of the labelled amount	100.0		100.2		101.0		99.9		99.1	
Impurities/ Degradation Products Determination (%)	PSD-01404-1	Any known individual: NMT 0.1% Total Unknown Imp: NMT 0.5% Total known Imp: NMT 1.5% Total UNKNOWN	<u>RRT</u> 0.93 Imp.E 1.11 Imp.F	<u>%</u> <0.03 0.09 <0.03 0.04 0.13	<u>RRT</u> 0.93 Imp.E 1.10 Imp.F	<u>%</u> 0.03 0.09 <0.03 0.04 0.16	<u>RRT</u> 0.93 Imp.E 1.11 Imp.F	<u>%</u> <0.03 0.09 <0.03 0.04 0.13	<u>RRT</u> 0.93 Imp.E 1.11 Imp.F	<u>%</u> <0.03 0.06 <0.03 0.02 0.08	<u>RRT</u> 0.93 Imp.E 1.11 Imp.F	<u>%</u> <0.03 0.08 <0.04 0.04 0.15
Total Viable Count	Ph.Eur.	Aerobic bacteria (CFU/g): NMT 1000 Fungi count (CFU/g) NMT 100	< 1000 < 10		- -		< 1000 < 10				< 1000 < 10	
Test for specified micro-organism	Ph.Eur.	Absence of E. coli in 1 g of product	conforms		-		conforms				conforms	

HPLC Assay I Pseudoephedrine HCl 60mg - Percentage of Labelled Amount

HPLC Assay II Triprolidine HCl 2.5 mg - Percentage of Labelled Amount

STABILITY STUDIES -GENERIC ACTIFED TABLETS 60/2.5 mg**TRIPROLIDINE ASSAY**

Batch number: AIG/167-02-597
Batch size: 180,000 tablets
Manufacturing date: 28.04.1997.
Storage conditions: 25°C (±2°) / 60%RH (±5%)
Packaging: Blister: PVC / PVdC film laminate into Aluminium foil.
HPLC II Assay: Triprolidine 2.5mg/Tab - Percentage of labelled Amount

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Parameter ↻	Test	Specification	T₀		6 month		12 months		24 months		36 months	
Analysis date ↻	Method	Criteria Accept -Reject	21. May 1997		23. Nov 1997		24. May 1998		20. May 1999		27. May 2000	
Appearance Description Score	PSD-01400-0	White, round film-coated tablets 9.2 mm diameter, scored on one the face and plain on the reverse side.	Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface	
(%) Dissolution labeled amount	PSD-01402	NLT 75% of the labelled amount dissolves within 45 minutes	100.3		102.5		100.2		108.9		100.2	
Assay II (%)	PSD-01404	95.0 - 105.0% of the labelled amount	100.9		101.3		100.3		101.1		100.8	
Impurities/ Degradation Products Determination (%)	PSD-01404-1	Any known individual: NMT 0.1% Total Unknown Imp: NMT 0.5% Total known Imp: NMT 1.5%	RRT	N/D	RRT	N/D	RRT	N/D	RRT	N/D	RRT	N/D
Total Viable Count	Ph.Eur.	Aerobic bacteria (CFU/g): NMT 1000 Fungi count (CFU/g) NMT 100	< 1000 < 10		- -		< 1000 < 10				< 1000 < 10	
Test for specified micro-organism	Ph.Eur.	Absence of E. coli in 1 g of product	conforms		-		conforms				conforms	

STABILITY STUDIES -GENERIC ACTIFED TABLETS 60/2.5 mg

PSEUDOEPHEDRINE ASSAY

Batch number: AIG/167-02-597
Batch size: 180,000 tablets
Manufacturing date: 28.04.1997.
Storage conditions: 25°C (±2°) / 60%RH (±5%)
Packaging: HDPE Securitainer 30cc round white bottle -Quantum Resin LR-7340-43 - 29mm Techniplex cap
HPLC I Assay: Pseudoephedrine 60mg/Tab - Percentage of labelled Amount

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Parameter 	Test	Specification	T ₀	6 month	12 months	24 months	36 months			
Analysis date 	Method	Criteria Accept -Reject	21. May 1997	23. Nov 1997	24. May 1998	20. May 1999	27. May 2000			
Appearance Description Score	PSD-01400-0	White, round film-coated tablets 9.2 mm diameter, scored on one the face and plain on the reverse side.	Color conforms No spots or marks on coat smooth surface	Color conforms No spots or marks on coat smooth surface	Color conforms No spots or marks on coat smooth surface	Color conforms No spots or marks on coat smooth surface	Color conforms No spots or marks on coat smooth surface			
(%) Dissolution labeled amount	PSD-01402	NLT 75% of the labelled amount dissolves within 45 minutes	101.2	102.5	100.3	99.6	100.2			
Assay I (%)	PSD-01404	95.0 - 105.0% of the labelled amount	97.3	98.7	99.3	100.7	100.9			
Impurities/ Degradation Products Determination (%)	PSD-01404-1	Any known individual: NMT 0.1% Total Unknown Imp: NMT 0.5% Total known Imp: NMT 1.5% Total UNKNOWN	<u>RRT</u> 0.93 Imp.E 1.11 Imp.F 0.13	<u>%</u> <0.03 0.09 <0.03 0.04 0.14	<u>RRT</u> 0.93 Imp.E 1.10 Imp.F 0.14	<u>%</u> 0.03 0.10 <0.03 0.04 0.13	<u>RRT</u> 0.93 Imp.E 1.11 Imp.F 0.10	<u>%</u> <0.03 0.07 <0.02 0.03 0.10	<u>RRT</u> 0.93 Imp.E 1.11 Imp.F 0.13	<u>%</u> <0.03 0.09 <0.03 0.04 0.13
Total Viable Count	Ph.Eur.	Aerobic bacteria (CFU/g): NMT 1000 Fungi count (CFU/g) NMT 100	< 1000 < 10	- -	< 1000 < 10		< 1000 < 10			
Test for specified micro-organism	Ph.Eur.	Absence of E. coli in 1 g of product	conforms	-	conforms		conforms			

STABILITY STUDIES -GENERIC ACTIFED TABLETS 60/2.5 mg

TRIPROLIDINE ASSAY

Batch number: AIG/167-02-597
Batch size: 180,000 tablets
Manufacturing date: 28.04.1997.
Storage conditions: 25°C (±2°) / 60%RH (±5%)
Packaging: HDPE Securitainer 30cc round white bottle -Quantum Resin LR-7340-43 - 29mm Techniplex cap
HPLC II Assay Triprolidine 2.5mg/Tab - Percentage of labelled Amount

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Parameter 	Test	Specification	T ₀		6 month		12 months		24 months		36 months	
Analysis date 	Method	Criteria Accept -Reject	21. May 1997		23. Nov 1997		24. May 1998		20. May 1999		27. May 2000	
Appearance Description Score	PSD-01400-0	White, round film-coated tablets 9.2 mm diameter, scored on one the face and plain on the reverse side.	Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface		Color conforms No spots or marks on coat smooth surface	
(%) Dissolution labeled amount	PSD-01402	NLT 75% of the labelled amount dissolves within 45 minutes	99.4		101.1		100.1		101.2		100.2	
Assay II (%)	PSD-01404	95.0 - 105.0% of the labelled amount	98.4		98.8		99.5		100.9		98.5	
Impurities/ Degradation Products Determination (%)	PSD-01404-1	Any known individual: NMT 0.1% Total Unknown Imp: NMT 0.5% Total known Imp: NMT 1.5%	RRT	N/D	RRT	N/D	RRT	N/D	RRT	N/D	RRT	N/D
Total Viable Count (Euro Lot)	Ph.Eur.	Aerobic bacteria (CFU/g): NMT 1000 Fungi count (CFU/g) NMT 100	< 1000 < 10		- -		< 1000 < 10				< 1000 < 10	
Test for specified micro-organism	Ph.Eur.	Absence of E. coli in 1 g of product	conforms		-		conforms				conforms	

HPLC Assay I Pseudoephedrine HCl 60mg - Percentage of Labelled Amount
HPLC Assay II Triprolidine HCl 2.5 mg - Percentage of Labelled Amount .