DRUG DEVELOPMENT

Hand 20 01 Books

Drug **D**evelopment & **M**anufacture for **P**harmaceutical **T**echnology **P**rofessions

HANDBOOK OF GENERIC DRUG DEVELOPMENT

READY-To-GO™ *SERIES*

DRUG DEVELOPMENT

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Drug **D**evelopment & **M**anufacture for **P**harmaceutical **T**echnology **P**rofessions

TECHNICAL FILE

CMC

Part II

STABILITY

e-HANDBOOK of GENERIC DEVELOPMENT KNOW-HOW SERIES

01/99 Part No. HBGDPI-II-V1

DRUG DEVELOPMENT

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Drug **D**evelopment & **M**anufacture for **P**harmaceutical **T**echnology **P**rofessions

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**

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
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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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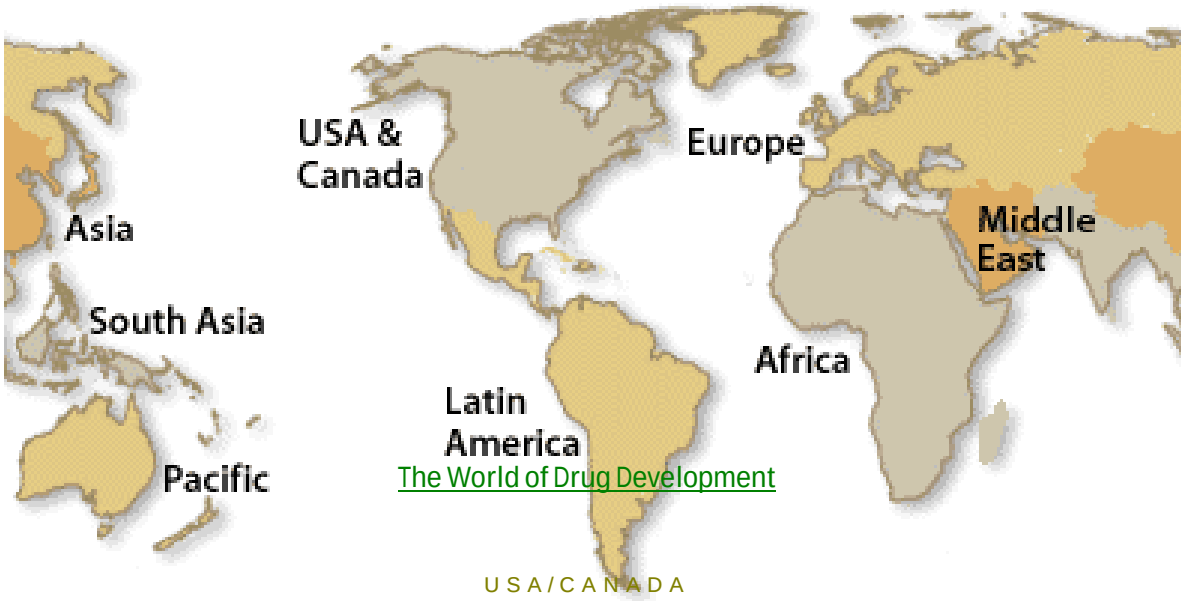

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Company
Responsible Officer

_____

For and on behalf of the purchasing Company

[FAX OR MAIL BACK THIS PAGE BEFORE USE]

Jennifer Anne Slemment

Authorized signature of Locum International marketing director

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research@IAGIM.org
info@locum.co.il

PRODUCT MASTER FORMULA

Generic Name: **Pseudoephedrine 60mg / Triprolidine 2.5mg Tablets**	**IAGIM**	Signatures ➲ Development	
	Edition No: 02	Validation ➲	
DEPARTMENT: Granulation & Tabletting	Edition Status: Spsds. 01	Production ➲	
PRECAUTION: Wear mask and gloves	Effective Date: **Jan/15/2001**	Q.A. ➲	
CAUTION: 1.Wear Masks with air filters 2.Potent Active Materials	Cat. No: **IAG-167-2000**	R.A. ➲	

CHANGE : No change

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	**91**	**220**					

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

ED. N0: 02 Replaces 01	Effective Date:	**APPROVED:**			
Ed. Status : 02 - EU	Jan / 15 / 2001	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

Parameter / Analysis date	Test / Method	Specification / Criteria Accept -Reject	T0 / 21. May 1997		6 month / 23. Nov 1997		12 months / 24. May 1998		24 months / 20. May 1999		36 months / 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%	**RRT** 0.93 Imp.E 1.11 Imp.F	**%** <0.03 0.09 <0.03 0.04	**RRT** 0.93 Imp.E 1.10 Imp.F	**%** 0.03 0.09 <0.03 0.04	**RRT** 0.93 Imp.E 1.11 Imp.F	**%** <0.03 0.09 <0.03 0.04	**RRT** 0.93 Imp.E 1.11 Imp.F	**%** <0.03 0.06 <0.03 0.02	**RRT** 0.93 Imp.E 1.11 Imp.F	**%** <0.03 0.08 <0.04 0.04
		Total UNKNOWN		0.13		0.16		0.13		0.08		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

Parameter / Analysis date	Test Method	Specification Criteria Accept -Reject	T0 21. May 1997	6 month 23. Nov 1997	12 months 24. May 1998	24 months 20. May 1999	36 months 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

Parameter / Analysis date	Test / Method	Specification / Criteria Accept -Reject	T0 / 21. May 1997	6 month / 23. Nov 1997	12 months / 24. May 1998	24 months / 20. May 1999	36 months / 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	RRT / % 0.93 <0.03 Imp.E 0.09 1.11 <0.03 Imp.F 0.04 0.13	RRT / % 0.93 0.03 Imp.E 0.10 1.10 <0.03 Imp.F 0.04 0.14	RRT / % 0.93 <0.03 Imp.E 0.09 1.11 <0.03 Imp.F 0.04 0.13	RRT / % 0.93 <0.03 Imp.E 0.07 1.11 <0.02 Imp.F 0.03 0.10	RRT / % 0.93 <0.03 Imp.E 0.09 1.11 <0.03 Imp.F 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

Parameter / Analysis date	Test / Method	Specification / Criteria Accept -Reject	T^0 / 21. May 1997	6 month / 23. Nov 1997	12 months / 24. May 1998	24 months / 20. May 1999	36 months / 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 .