

French National Agency for Medicines and Health Products Safety

CERTIFICATE NUMBER: 19MPP032HFR01

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER

Part 1

Issued following an inspection in accordance with:

Art. 111(5) of Directive 2001/83/EC as amended

The competent authority of France confirms the following:

The manufacturer: PCAS

Site address: 19 route de Meulan, LIMAY, 78520, France

Is an active substance manufacturer that has been inspected in accordance with Art. 111(1) of Directive 2001/83/EC.

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on **2019-03-07**, it is considered that it complies with:

• The principles of GMP for active substances ³ referred to in Article 47 of Directive 2001/83/EC.

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection. However, this period of validity may be reduced or extended using regulatory risk management principles by an entry in the Restrictions or Clarifying remarks field. This certificate is valid only when presented with all pages and both Parts 1 and 2. The authenticity of this certificate may be verified in EudraGMDP. If it does not appear, please contact the issuing authority.

¹ The certificate referred to in paragraph 111(5) of Directive 2001/83/EC and 80(5) of Directive 2001/82/EC, shall also be required for imports coming from third countries into a Member State.

² Guidance on the interpretation of this template can be found in the Help menu of EudraGMDP database.

³ These requirements fulfil the GMP recommendations of WHO.



Part 2

Manufacture of active substance. Names of substances subject to inspection:

ALIMEMAZINE TARTRATE(en)

CICLOPIROX OLAMINE(en)

CLOMIFENE CITRATE(en)

LEDIPASVIR(en)

MEPENZOLATE BROMIDE(en)

MOEXIPRIL HYDROCHLORIDE(en)

ESOMEPRAZOLE MAGNESIUM DIHYDRATE(en)

NIFURATEL(en)

OPIUM, STANDARDIZED POWDERED(en) - confidential

OXYBUTYNIN(en)

OXYBUTYNIN HYDROCHLORIDE(en)

PHOLCODINE (en) - confidential

PINDOLOL(en)

PIPERIDOLATE HYDROCHLORIDE(en

PIPER	PIPERIDOLATE HYDROCHLORIDE(en)		
3. MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES			
Activ	e Substance : ALIMEMAZINE TARTRATE		
3.1	Manufacture of Active Substance by Chemical Synthesis		
11-11-11-11-11	3.1.1 Manufacture of active substance intermediates		
	3.1.2 Manufacture of crude active substance		
	3.1.3 Salt formation / Purification steps :		
	Crystallization		
3.5	General Finishing Steps		
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material		
	which is in direct contact with the substance)		
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging		
	material or container. This also includes any labelling of the material which could be used for		
	identification or traceability (lot numbering) of the active substance)		
3.6	Quality Control Testing		
	3.6.1 Physical / Chemical testing		
Activ	e Substance : CICLOPIROX OLAMINE		
3.1	Manufacture of Active Substance by Chemical Synthesis		
	3.1.1 Manufacture of active substance intermediates		
	3.1.2 Manufacture of crude active substance		
	3.1.3 Salt formation / Purification steps:		
	Crystallization		
3.5	General Finishing Steps		
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material		
	which is in direct contact with the substance)		
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging		



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	gence nationale de sécurité du médicament l des produits de santé material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
	e Substance : CLOMIFENE CITRATE
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
3.5	Crystallization General Finishing Steps
3.3	。 第一章 "我们就是我们的,我们就是我们的,我们就是我们的,我们就是我们的,我们就是我们的,我们就是我们的,我们就是我们的,我们就是我们的,我们就是什么的。
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Harasa Tana	e Substance : LEDIPASVIR
2.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.1 Manufacture of active substance intermediates General Finishing Steps
	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for
3.5	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
3.5	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.5 3.6	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing 3.6.1 Physical / Chemical testing
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3.5 3.6	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing 3.6.1 Physical / Chemical testing
3.5 3.6	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing 3.6.1 Physical / Chemical testing e Substance : MEPENZOLATE BROMIDE Manufacture of Active Substance by Chemical Synthesis
3.5 3.6	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing 3.6.1 Physical / Chemical testing Bubstance: MEPENZOLATE BROMIDE Manufacture of Active Substance by Chemical Synthesis 3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps:
3.5 3.6 active	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing 3.6.1 Physical / Chemical testing e Substance : MEPENZOLATE BROMIDE Manufacture of Active Substance by Chemical Synthesis 3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : Centrifugation
3.5 3.6 Active	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing 3.6.1 Physical / Chemical testing Bubstance: MEPENZOLATE BROMIDE Manufacture of Active Substance by Chemical Synthesis 3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps:
3.5 3.6 Active	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing 3.6.1 Physical / Chemical testing e Substance : MEPENZOLATE BROMIDE Manufacture of Active Substance by Chemical Synthesis 3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : Centrifugation
3.5 3.6 Active	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing 3.6.1 Physical / Chemical testing e Substance : MEPENZOLATE BROMIDE Manufacture of Active Substance by Chemical Synthesis 3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : Centrifugation General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.5	3.1.1 Manufacture of active substance intermediates General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing 3.6.1 Physical / Chemical testing e Substance: MEPENZOLATE BROMIDE Manufacture of Active Substance by Chemical Synthesis 3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps: Centrifugation General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material)

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Ac	gence nationale de sécurité du médicament des produits de santé identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
is a partitud	3.6.1 Physical / Chemical testing
	e Substance : MOEXIPRIL HYDROCHLORIDE
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates3.1.2 Manufacture of crude active substance
	3.1.2 Maintracture of Crude active substance 3.1.3 Salt formation / Purification steps:
	Crystallization
3.5	General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
	e Substance : ESOMEPRAZOLE MAGNESIUM DIHYDRATE
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance3.1.3 Salt formation / Purification steps :
	Centrifugation
3.5	General Finishing Steps
Dekter Fa	3.5.1 Physical processing steps :
	Micronization
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active	e Substance : NIFURATEL
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : Centrifugation
3.5	General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)



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et	rence nationale de sécurité du médicament des produits de santé 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
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***	e Substance : OPIUM, STANDARDIZED POWDERED - confidential
3.5	General Finishing Steps
	3.5.1 Physical processing steps :
	Standardisation
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
ESTANCE AND SE	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Activ	e Substance : OXYBUTYNIN
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Crystallization
3.5	General Finishing Steps
A BOTH ACTION	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Activ	e Substance : OXYBUTYNIN HYDROCHLORIDE
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Recrystallization
3.5	General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for



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3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active	e Substance : PHOLCODINE - confidential
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Crystallization
3.5	General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
26	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active	e Substance : PINDOLOL
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Crystallization
3.5	General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
3.6	identification or traceability (lot numbering) of the active substance) Quality Control Testing
3.6	
	3.6.1 Physical / Chemical testing
Active	e Substance : PIPERIDOLATE HYDROCHLORIDE
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
,	Crystallization
3.5	General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
l I	material or container. This also includes any labelling of the material which could be used for

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	nence nationale de sécurité du médicament de produits de santé l'acceptable de
3.6	Quality Control Testing
45-2-5-2-5-111-2-	3.6.1 Physical / Chemical testing

Any restrictions related to the scope of this certificate:

LEDIPASVIR: limited to the manufacture of the Azabicyclobenzimidazole intermediate

Clarifying remarks (for public users)

ALIMEMAZINE TARTRATE: TRIMEPRAZINE TARTRATE = ALIMEMAZINE TARTRATE; ESOMEPRAZOLE MAGNESIUM DIHYDRATE manufactured from omeprazole

2019-06-06

Name and signature of the authorised person of the Competent Authority of France

Mr. Guillaume Renaud

French National Agency for Medicines and Health

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