*Agenzia Italiana del Farmaco*

CERTIFICATE NUMBER: ***IT-API/144/H/2015***

# CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER [1, 2]

**Part 1**

Issued following an inspection in accordance with :
Art. 111(5) of Directive 2001/83/EC as amended

The competent authority of Italy confirms the following:
The manufacturer: ***LUSOCHIMICA S.P.A.***
Site address: ***Via Livornese, 897, PISA, 56122, Italy***

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 ***2015-07-23*** , 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 EudraGMP. 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**

| Human Medicinal Products |
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Manufacture of active substance. Names of substances subject to inspection :
***DEXKETOPROFENE ACIDO( it) / DEXKETOPROFEN ACID( en)***
***FORMOTEROLO FUMARATO DIIDRATO( it) / FORMOTEROL FUMARATE DIHYDRATE( en)***
***MANIDIPINA DICLORIDRATO( it) / MANIDIPINE DIHYDROCHLORIDE( en)***
***MEPIFILLINA( it) / MEPIFILINE( en)***
***ROCIVERINA( it) / ROCIVERINE( en)***
***DEXKETOPROFENE TROMETAMOLO( it) / DEXKETOPROFEN TROMETAMOL( en)***
***CAPTOPRIL( it) / CAPTOPRIL( en)***
***GLIBENCLAMIDE( it) / GLIBENCLAMIDE( en)***
***ZOFENOPRIL CALCIO( it) / ZOFENOPRIL CALCIUM( en)***
***BENIDIPINA CLORIDRATO( it) / BENIDIPINE HYDROCHLORIDE( en)***
***FOSINOPRIL SALE SODICO( it) / FOSINOPRIL SODIUM SALT( en)***
***IBODUTANT( it) / IBODUTANT( en)***

**3. MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES**

Active Substance : DEXKETOPROFEN ACID

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| **3.1** | **Manufacture of Active Substance by Chemical Synthesis** |
| | 3.1.3 Salt formation / Purification steps :<br>crystallisation<br>3.1.2 Manufacture of crude active substance |
| **3.5** | **General Finishing Steps** |
| | 3.5.1 Physical processing steps :<br>drying<br>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)<br>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) |
| **3.6** | **Quality Control Testing** |
| | 3.6.1 Physical / Chemical testing |

Active Substance : FORMOTEROL FUMARATE DIHYDRATE

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| **3.1** | **Manufacture of Active Substance by Chemical Synthesis** |
| | 3.1.3 Salt formation / Purification steps :<br>crystallisation<br>3.1.2 Manufacture of crude active substance |
| **3.5** | **General Finishing Steps** |
| | 3.5.1 Physical processing steps :<br>drying<br>3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging |

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| | 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)<br>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) |

Active Substance : MANIDIPINE DIHYDROCHLORIDE

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| **3.1** | **Manufacture of Active Substance by Chemical Synthesis** |
| | 3.1.3 Salt formation / Purification steps :<br>crystallisation<br>3.1.2 Manufacture of crude active substance |
| **3.5** | **General Finishing Steps** |
| | 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)<br>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)<br>3.5.1 Physical processing steps :<br>drying,milling |

Active Substance : MEPIFILINE

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| **3.1** | **Manufacture of Active Substance by Chemical Synthesis** |
| | 3.1.3 Salt formation / Purification steps :<br>crystallisation |
| **3.5** | **General Finishing Steps** |
| | 3.5.1 Physical processing steps :<br>drying<br>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)<br>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) |
| **3.6** | **Quality Control Testing** |
| | 3.6.1 Physical / Chemical testing |

Active Substance : ROCIVERINE

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| **3.1** | **Manufacture of Active Substance by Chemical Synthesis** |
| | 3.1.3 Salt formation / Purification steps :<br>salt formation<br>3.1.2 Manufacture of crude active substance |
| **3.5** | **General Finishing Steps** |
| | 3.5.1 Physical processing steps :<br>distillation<br>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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| **3.6** | **Quality Control Testing** |
| | 3.6.1 Physical / Chemical testing |

Active Substance : DEXKETOPROFEN TROMETAMOL

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| **3.1** | **Manufacture of Active Substance by Chemical Synthesis** |
| | 3.1.1 Manufacture of active substance intermediates<br>3.1.3 Salt formation / Purification steps :<br>salt formation,crystallisation |
| **3.5** | **General Finishing Steps** |
| | 3.5.1 Physical processing steps :<br>drying<br>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)<br>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) |
| **3.6** | **Quality Control Testing** |
| | 3.6.1 Physical / Chemical testing |

Active Substance : CAPTOPRIL

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| **3.1** | **Manufacture of Active Substance by Chemical Synthesis** |
| | 3.1.3 Salt formation / Purification steps :<br>crystallisation<br>3.1.2 Manufacture of crude active substance |
| **3.5** | **General Finishing Steps** |
| | 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)<br>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)<br>3.5.1 Physical processing steps :<br>drying,milling |
| **3.6** | **Quality Control Testing** |
| | 3.6.1 Physical / Chemical testing |

Active Substance : GLIBENCLAMIDE

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| **3.1** | **Manufacture of Active Substance by Chemical Synthesis** |
| | 3.1.3 Salt formation / Purification steps :<br>crystallisation<br>3.1.1 Manufacture of active substance intermediates |
| **3.5** | **General Finishing Steps** |
| | 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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| | identification or traceability (lot numbering) of the active substance)<br>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)<br>3.5.1 Physical processing steps :<br>drying,milling |
| **3.6** | **Quality Control Testing** |
| | 3.6.1 Physical / Chemical testing |

Active Substance : ZOFENOPRIL CALCIUM

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| **3.1** | **Manufacture of Active Substance by Chemical Synthesis** |
| | 3.1.3 Salt formation / Purification steps :<br>crystallisation<br>3.1.1 Manufacture of active substance intermediates |
| **3.5** | **General Finishing Steps** |
| | 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)<br>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)<br>3.5.1 Physical processing steps :<br>drying,milling/micronisation |
| **3.6** | **Quality Control Testing** |
| | 3.6.1 Physical / Chemical testing |

Active Substance : BENIDIPINE HYDROCHLORIDE

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| **3.1** | **Manufacture of Active Substance by Chemical Synthesis** |
| | 3.1.3 Salt formation / Purification steps :<br>crystallisation<br>3.1.2 Manufacture of crude active substance |
| **3.5** | **General Finishing Steps** |
| | 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)<br>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)<br>3.5.1 Physical processing steps :<br>drying,milling |
| **3.6** | **Quality Control Testing** |
| | 3.6.1 Physical / Chemical testing |

Active Substance : FOSINOPRIL SODIUM SALT

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| **3.1** | **Manufacture of Active Substance by Chemical Synthesis** |
| | 3.1.3 Salt formation / Purification steps : |

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| | crystallisation<br>3.1.2 Manufacture of crude active substance |
| **3.5** | **General Finishing Steps** |
| | 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)<br>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)<br>3.5.1 Physical processing steps :<br>drying,milling |
| **3.6** | **Quality Control Testing** |
| | 3.6.1 Physical / Chemical testing |
| Active Substance : IBODUTANT | |
| **3.1** | **Manufacture of Active Substance by Chemical Synthesis** |
| | 3.1.3 Salt formation / Purification steps :<br>crystallisation<br>3.1.2 Manufacture of crude active substance |
| **3.5** | **General Finishing Steps** |
| | 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)<br>3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)<br>3.5.1 Physical processing steps :<br>drying,milling |
| **3.6** | **Quality Control Testing** |
| | 3.6.1 Physical / Chemical testing |

4. Other Activities - Active Substances :
***Importation of: THEOPHYLLINE-7-ACETIC ACID (confidential), CHLORPROPAMIDE (confidential), MEPYRAMINE (confidential), TROMETAMOL (confidential)***

Clarifying remarks (for public users)

***Imported active substances marked as confidential undergo further processing within the importing site.The Inspectorate adopted a risk-based approach for planning of inspections, therefore the validity of the GMP certificate for this manufacturing site is not more than¿ 42 months from the last general GMP inspection, which was conducted on (2015/July/23). It will still be AIFA's right to re-evaluate the validity of the GMP certificate based on risk profile changes.No Batch certification for: Manidipinba Dicloridrato e Formeterolo Fumarato Diidrato***

*2015-12-18*

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

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***Confidential***
***Agenzia Italiana del Farmaco***
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