Javna agencija Republike Slovenije za zdravila in medicinske pripomočke

CERTIFICATE NUMBER : ***450-38/2017-1***

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
Art. 80(5) of Directive 2001/82/EC as amended

The competent authority of Slovenia confirms the following:

The manufacturer : ***Lek d.d., PE PROIZVODNJA MENGEŠ***

Site address : ***Kolodvorska cesta 27, Mengeš, 1234, Slovenia***

Is an active substance manufacturer that has been inspected in accordance with Art. 111(1) of Directive 2001/83/EC and Art. 80(1) of Directive 2001/82/EC .

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2017-04-13*** , 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 and Article 51 of Directive 2001/82/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.

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(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 :
[11160] AMLODIPINE BESILATE (en)
[11161] ATORVASTATINE CALCIUM (en)
[15210] BROMOCRIPTINE MESYLATE (en)
[11186] CANDESARTAN CILEXETIL (en)
[11164] LITHIUM CARBONATE (en)
[15212] MYCOPHENOLATE MOFETIL (en)
[11168] NITROXOLINE (en)
[11170] OMEPRAZOL SODIUM (en)
[14841] PERINDOPRIL ERBUMIN (en)
[11179] ROSUVASTATIN CA (en)
[11174] SILVER SULFADIAZINE (en)
[11175] TACROLIMUS (en)
[15213] TAMSULOSIN HCL (en)
[15215] VANCOMYCIN HYDROCHLORIDE (en)
[11177] TOLTERODIN TARTRATE (en)
EVEROLIMUS (en)
[jazmp] RAPAMYCINE (en)
[jazmp1] ATORVARSTATINE CALCIUM FORM I (en)
[jazmp3] FESOTERODIN (en)
FERUMOXYTOL (en)
[jazmp4] S-OMEPRAZOLE MG DIHYDRAT (en)
PIMECROLIMUS (en)
[jazmp20] PLANT EXTRACT-ECHINACEA (en)
[JAZMP51] BENZYLOXY-CHLOROETHANOL-QUINOLINONE (en)
[JAZMP52] BENZYLOXY-OXIRANYL-QUINOLINONE (en)

3. MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES	
Active Substance : AMLODIPINE BESILATE	
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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing
Active Substance : ATORVASTATINE CALCIUM	
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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : BROMOCRIPTINE MESYLATE

3.3	**Manufacturing of Active Substance using Biological Processes**
	3.3.1 Fermentation 3.3.3 Isolation / Purification
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : salt formation, crystalization, milling/micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : CANDESARTAN CILEXETIL

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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : LITHIUM CARBONATE

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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : MYCOPHENOLATE MOFETIL

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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : NITROXOLINE

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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : OMEPRAZOL SODIUM

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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : PERINDOPRIL ERBUMIN

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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : ROSUVASTATIN CA

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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : SILVER SULFADIAZINE

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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : TACROLIMUS

3.3	**Manufacturing of Active Substance using Biological Processes**
	3.3.1 Fermentation 3.3.3 Isolation / Purification 3.3.5 Other : Chromatography and crystallization
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : Blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : TAMSULOSIN HCL

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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : VANCOMYCIN HYDROCHLORIDE

3.3	**Manufacturing of Active Substance using Biological Processes**
	3.3.1 Fermentation 3.3.3 Isolation / Purification
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : salt formation, crystalization 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : TOLTERODIN TARTRATE

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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : EVEROLIMUS

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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : RAPAMYCINE

3.3	**Manufacturing of Active Substance using Biological Processes**
	3.3.1 Fermentation 3.3.3 Isolation / Purification 3.3.5 Other : Chromatography and crystallization
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : Milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : ATORVARSTATINE CALCIUM FORM I

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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : FESOTERODIN

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**

	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : FERUMOXYTOL

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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : S-OMEPRAZOLE MG DIHYDRAT

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**
	3.5.1 Physical processing steps : milling, micronization and blending 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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : PIMECROLIMUS

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 : crystalization
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : milling, micronization, blending 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 Substance : PLANT EXTRACT-ECHINACEA

3.2	**Extraction of Active Substance from Natural Sources**
	3.2.1 Extraction of substance from plant source
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 3.6.2 Microbiological testing excluding sterility testing

Active Substance : BENZYLOXY-CHLOROETHANOL-QUINOLINONE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : drying 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 Substance : BENZYLOXY-OXIRANYL-QUINOLINONE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.1 Manufacture of active substance intermediates
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : drying 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

2017-09-25

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

Confidential

Agency for medicinal products and medical devices of the Republic of Slovenia

Tel : ***Confidential***

Fax : ***Confidential***