Agenzia Italiana del Farmaco

CERTIFICATE NUMBER :***IT-API/229/H/2020***

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:***OLON S.P.A.***
Site address:***VIA DELLA VITTORIA, 89, MULAZZANO, 26837, 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 ***2020-01-24*** , 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.

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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

Human Medicinal Products

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

ACICLOVIR(en)
VALGANCICLOVIR HYDROCHLORIDE(en)
BICALUTAMIDE(en)
RIFAMPICIN(en)
FUROSEMIDE(en)
ACAMPROSATE CALCIUM(en)
MINOXIDIL(en)
RALOXIFENE HYDROCHLORIDE(en)
RIFAMYCIN SODIUM(en)
RIFAXIMIN(en)
BUPROPION HYDROCHLORIDE(en)
OXAPROZIN(en)
CLOBENZOREX HYDROCHLORIDE(en)
ATAZANAVIR SULFATE(en)
TAMOXIFEN CITRATE(en)
OSPEMIFENE(en)
CRUDE DICLOFENAC SODIUM(en)
HYDROXYCARBAMIDE(en)
FENOFIBRATE(en)
TOREMIFENE CITRATE(en)
GLUCOSE 1-PHOSPHATE DISODIUM(en)

3. MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES

Active Substance :ACICLOVIR

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.3 Salt formation / Purification steps: crystallisation 3.1.2 Manufacture of crude active substance 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) 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.1 Physical processing steps: drying,milling,sieving
3.6	**Quality Control Testing**
	3.6.2 Microbiological testing excluding sterility testing 3.6.1 Physical / Chemical testing

Active Substance :VALGANCICLOVIR HYDROCHLORIDE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.3 Salt formation / Purification steps: crystallisation 3.1.2 Manufacture of crude active substance 3.1.1 Manufacture of active substance intermediates
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps: spray drying 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) 3.5.2 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 :BICALUTAMIDE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.3 Salt formation / Purification steps: crystallisation 3.1.2 Manufacture of crude active substance 3.1.1 Manufacture of active substance intermediates *Special Requirements :* 7.Other: Other: Hormones or substances with hormonal activity
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) 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.1 Physical processing steps: drying,milling,micronisation
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing

Active Substance :RIFAMPICIN

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

Active Substance :FUROSEMIDE

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

Active Substance :ACAMPROSATE CALCIUM

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

Active Substance :MINOXIDIL

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

Active Substance :RALOXIFENE HYDROCHLORIDE

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

Active Substance :RIFAMYCIN SODIUM

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.3 Salt formation / Purification steps: crystallisation
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) 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.1 Physical processing steps:

	drying,sieving
3.6	**Quality Control Testing**
	3.6.2 Microbiological testing excluding sterility testing 3.6.1 Physical / Chemical testing

Active Substance :RIFAXIMIN

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

Active Substance :BUPROPION HYDROCHLORIDE

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

Active Substance :OXAPROZIN

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

Active Substance :CLOBENZOREX HYDROCHLORIDE

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

Active Substance :ATAZANAVIR SULFATE

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

Active Substance :TAMOXIFEN CITRATE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.3 Salt formation / Purification steps: crystallisation 3.1.2 Manufacture of crude active substance 3.1.1 Manufacture of active substance intermediates *Special Requirements :* 7.Other: Other: Hormones or substances with hormonal activity
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) 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.1 Physical processing steps: drying, granulation,sieving,milling/micronisation
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing

Active Substance :OSPEMIFENE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.3 Salt formation / Purification steps: crystallisation 3.1.2 Manufacture of crude active substance 3.1.1 Manufacture of active substance intermediates *Special Requirements :* 7.Other: Other: Hormones or substances with hormonal activity
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) 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.1 Physical processing steps: drying,milling,sieving
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing

Active Substance :CRUDE DICLOFENAC SODIUM

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	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) 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 :HYDROXYCARBAMIDE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.3 Salt formation / Purification steps: crystallisation 3.1.2 Manufacture of crude active substance *Special Requirements :* 7.Other: Other: Cytotoxic
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) 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.1 Physical processing steps: drying,sieving
3.6	**Quality Control Testing**
	3.6.2 Microbiological testing excluding sterility testing 3.6.1 Physical / Chemical testing

Active Substance :FENOFIBRATE

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

Active Substance :TOREMIFENE CITRATE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.3 Salt formation / Purification steps: crystallisation 3.1.2 Manufacture of crude active substance 3.1.1 Manufacture of active substance intermediates *Special Requirements :* 7.Other: Other: Hormones or substances with hormonal activity
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) 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.1 Physical processing steps: drying,milling,sieving
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing
Active Substance :GLUCOSE 1-PHOSPHATE DISODIUM	
3.2	**Extraction of Active Substance from Natural Sources**
	3.2.6 Purification of extracted substance Plant 3.2.5 Modification of extracted substance Plant
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps: drying 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) 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.6	**Quality Control Testing**
	3.6.2 Microbiological testing excluding sterility testing 3.6.1 Physical / Chemical testing

4. Other Activities - Active Substances :

Importation of: FUROSEMIDE SODIUM (confidential), HOMOTAURINE (confidential), RIFAMYCIN O (confidential)

Clarifying remarks (for public users)

Manufactured active substances (AS) marked as confidential are for clinical use only. Imported AS marked as confidential undergo further processing within the importing site and/or are released to other AS manufacturing sites for processing. On a risk-based approach, the validity of the GMP certificate for this manufacturing site is not more than 36 months from the latest general GMP inspection conducted on 2020/01/24, except for AIFA¿s re-evaluation of the risk profile.

2020-12-03

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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