AGENZIA ITALIANA DEL FARMACO

Certificate No: IT-API/97/H/2019

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER

Part 1

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

The competent authority of Italy confirms the following:
The manufacturer HUVEPHARMA ITALIA SOCIETA' A RESPONSABILITA' LIMITATA
Site address Via R. Lepetit 142 - 12075 GARESSIO (CN)

Is an active substance manufacturer that has been inspected in accordance with Art. 111(1) of Directive 2001/83/EC transposed in the following national legislation: **D.L. n. 219 of 24th April 2006 art. 53**

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on 2018/10/12, it is considered that it complies with the Good Manufacturing Practice requirements referred to in the principles of GMP for active substances 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.
The authenticity of this certificate may be verified in Eudra GMDP. If it does not appear, please contact the issuing authority.

AIFA - Italian Medicines Agency
GMP Inspections and Manufacturing Authorizations of APIs Office
Via del Tritone, n° 181 - 00187 ROMA (ITALY)
Tel.+39065978401 Fax +390659784617
website: www.agenziafarmaco.it
SIS : 4245

VI
GMP

Part 2

Name and address of the site:

HUVEPHARMA ITALIA SOCIETA' A RESPONSABILITA' LIMITATA - Via R. Lepetit 142, 12075 GARESSIO (CN)

Name of the active Substances manufactured or imported:

ARTEMISININ
ARTESUNATE
L-ALANINE
OXYBUTYNIN HYDROCHLORIDE
POTASSIUM N-ACETYLAMINO SUCCINATE
SULPIRIDE
TIAPRIDE HYDROCHLORIDE
VIGABATRIN

3 - Manufacturing Operations - Active Substances

ARTEMISININ

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: Crystallisation
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

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	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 - Manufacturing Operations - Active Substances

ARTESUNATE

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: Crystallisation
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

3 - Manufacturing Operations - Active Substances

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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: Salt formation, crystallisation
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

3 - Manufacturing Operations - Active Substances

POTASSIUM N-ACETYLAMINO SUCCINATE

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: salt formation, crystallisation
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps centrifugation, drying, milling **3.5.2.** Primary Packaging (enclosing / sealing the active substance within a

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	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 - Manufacturing Operations - Active Substances

SULPIRIDE

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: crystallisation
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps drying,milling **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

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3 - Manufacturing Operations - Active Substances

TIAPRIDE 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: crystallisation,salt formation
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

3 - Manufacturing Operations - Active Substances

VIGABATRIN

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.2. Manufacture of crude active substance **3.1.3.** Salt formation / Purification steps: Crystallisation
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps

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	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

4. Other Activities - Active Substance:

Importation of:
L-ALANINE (Confidential)

Restrictions or clarifying remarks:

All imported APIs undergo further processing within the importing site only. 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 36 months from the last general GMP inspection, which was conducted on 2018/10/12. It will still be AIFA's right to re-evaluate the validity of the GMP certificate based on risk profile changes.

Rome, 2019/05/28

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

Dott.ssa Marisa Delbò
AIFA - GMP Inspections and Manufacturing Authorizations of APIs Office

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AGENZIA ITALIANA DEL FARMACO

This is a certified copy of the certificate issued on 2019/05/28 consisting of 8 sheets; the validity of the reprinted GMP certificate is the same as the original certificate and is indicated in paragraph Restriction or clarifying remarks.

For ratification

Aifa-GMP Inspection and Manufacturing Authorizations of APIs Office
Dott.ssa Marisa Delbò

Marisa Delbò

Rome, 2019/06/13

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Prefettura -Ufficio Territoriale del Governo di Roma

Legalizzazione Area IV Quinquies

Apostille **(Convention de La Haye du 5 octobre 1961)**	
1. Stato (Country/Pays/Pais):	**ITALIA**
il presente atto pubblico (This public document / Le preséntancte public / El presente documento público)	
2. E' stato firmato da: (Has been signed by/A été signé par/ Ha sido firmado por)	**DELBO' MARISA**
3. Operante in Qualità di : (Acting in the capacity of/Agissant en qualité de/Quein actue en calidad de)	**DIRIGENTE**
4. E' munito del sigillo/bollo di : (Bears the seal/stamp of/Est revêtu du sceac/ timbre de / Y esta' revestito del sello/ timbre de)	**AIFA - AGENZIA ITALIANA DEL FARMACO**
Attestato (Certified/Attesté/Certificado)	
5. in: Roma (At/A'/En)	**6. il: 07/11/2019 11:07** (On/Le/El dia)
7. da: Prefettura di Roma - Ufficio Territoriale del Governo di Roma (Precture of Rome - Local Governement in Rome / Préfecture de Rome - Le gouvernement local à Rome / Prefectura de Roma - Gabierno Local en Roma	
8. col numero (No / Sous no / Bajo el nùmero)	**16511 / 2019**
9. Sigillo / Bollo (Seal / Stamp / Sceau / Timbre / Sello / Timbre)	
10. Firma (Signature) **FUNZIONARIO DELEGATO** **ANNA RITA NUNZI**	

Questa Apostille certifica solo la qualità del firmatario e il sigillo che é stato apposto. Non certifica il contenuto del documento per il quale é stata rilasciata

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